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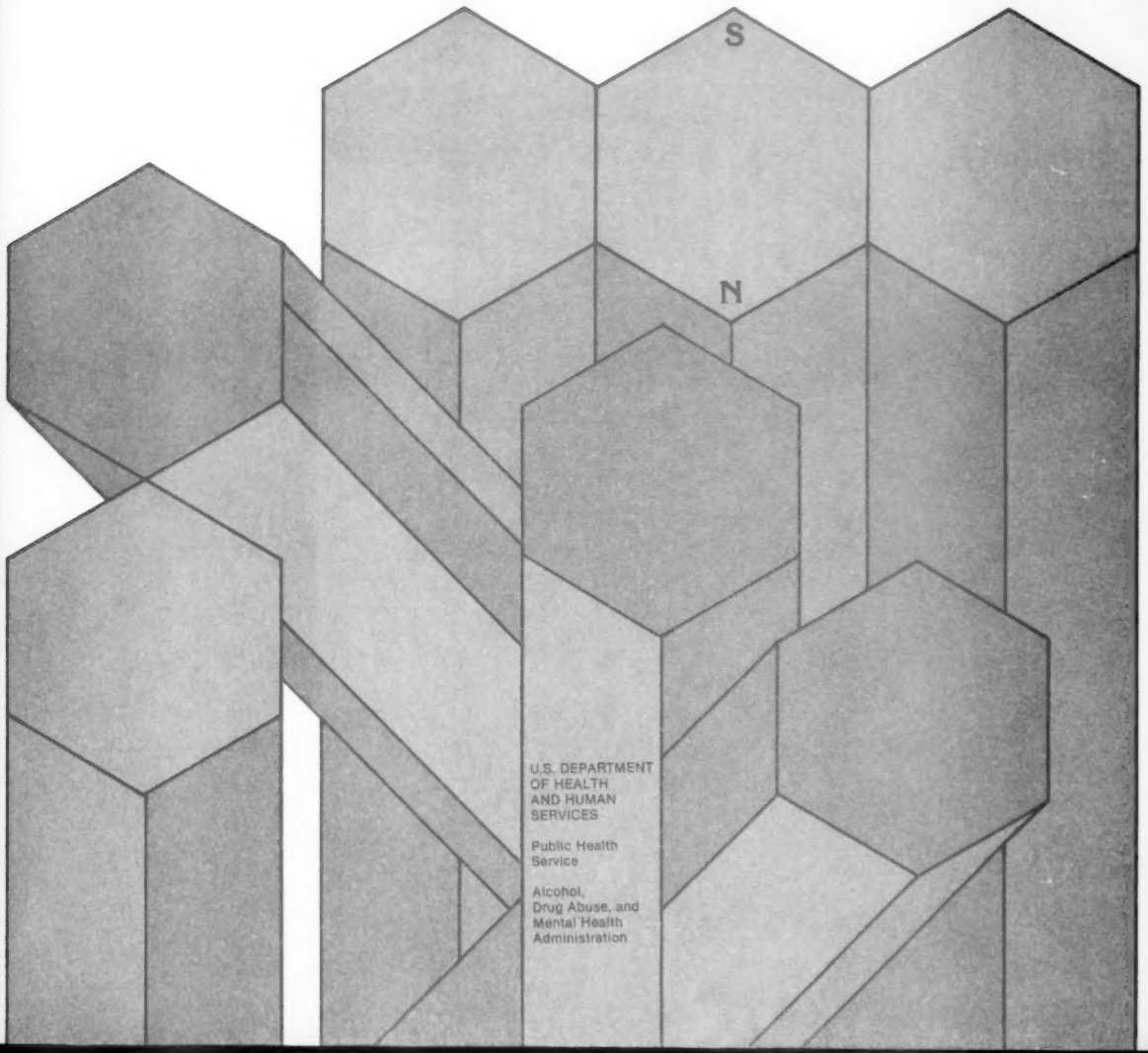

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Volume 18, Number 4 April 1981

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Carrie Lee Rothgeb, *Editor*
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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

003856 Ellefson, Charles R.; Prodan, Kathleen A.; Brougham, Linda R.; Miller, Arni. G. D. Searle and Co., Chicago, IL 60680 **Synthesis of 8-aryltetrahydroisoquinolines as dopamine antagonists and evaluation for potential neuroleptic activity.** Journal of Medicinal Chemistry. 23(9):977-980, 1980.

The synthesis of 8-(methoxyphenyl)-1,2,3,4-tetrahydroisoquinolines using aryloxazolines as key intermediates is described. Nucleophilic displacement on an o-methoxyphenyloxazoline by an aryl Grignard reagent, followed by electrophilic substitution at the other ortho position, provided a specific route to the properly substituted benzene intermediates necessary for conversion to the tetrahydroisoquinolines. These compounds and 8-phenyl- and 2-methyl-8-phenyl-1,2,3,4-tetrahydroisoquinolines, which are ring opened analogues of apomorphine, were found to be dopamine antagonists by in vitro dopamine receptor studies. In vivo evaluation, however, did not substantiate potential usefulness as antipsychotic agents when they were compared with standard neuroleptic agents. (Author abstract)

003857 Hjorth, S.; Carlsson, A.; Lindberg, P. Dept. of Pharmacology, University of Goteborg, Goteborg, Sweden **A new centrally acting DA-receptor agonist with selectivity for autoreceptors.** Psychopharmacology Bulletin. 16(3):85-90, 1980.

The synthesis of the dopamine (DA) analogue N-n-propyl-3-(3-hydroxyphenyl)-piperidine (3-PPP) while searching for new direct DA receptor agonists is described, and its unique pharmacological profile is discussed. Results of a series of in vivo and in vitro, anatomical and behavioral studies indicate that 3-PPP appears to be a centrally acting, selective D autoreceptor agonist. It is noted that 3-PPP may prove useful as a tool for elucidating dopaminergic functions and in the treatment of psychotic disorders and other disease states possibly associated with disturbances in central DA transmission. 6 references.

003858 Johnson, David Allan. University of California, San Francisco **Mechanism of drug action: examination of possible involvement of lipids in the action of 5-hydroxytryptamine and morphine. (Ph.D. dissertation).** Dissertation Abstracts International. 40(6):2629-B, 1979. Ann Arbor, Univ. Microfilms No. 7926646, 80p., 1978.

The possible involvement of lipids in the action of 5-hydroxytryptamine (5-HT) and morphine was examined. It was demonstrated that the acidic lipids cerebroside sulfate (CS), 1-phosphatidylinositol (PI), 1PI 4-phosphate (DPI), 1-PI 4,5-biphosphate (TPI), phosphatidic acid (PA), and phosphatidylserine (PS) can bind to tritiated 5-HT saturably and with high affinity in isobutanol, and that the 5-HT receptor isolated with Sephadex LH-20 contains at least two acidic lipids, CS and PI, which account for 90% of the observed binding activity in this preparation. In an aqueous environment, the affinities of 5-HT for CS, PI, DPI, TPI, PA, and PS were observed to be in general much lower and poorly correlated with values measured in isobutanol, suggesting that these lipids are probably not 5-HT receptors. In a second study, even 1mM morphine failed to alter the fluorescence polarization of 1,6-diphenylhexatriene (DPH) incorporated into bilayers composed of brain lipids, indicating that there were no alterations in bulk hydrocarbon fluid. Because measurement of the fluorescence depolarization of DPH monitors the bulk hydrocarbon region and differential scanning calorimetry (DSC) monitors the whole system, including lipid/lipid, lipid/protein, and protein/protein interactions, data tend to suggest that the alterations in phase transitions observed with DSC may be due to changes in the melting of proteins or proteins interacting with lipids and not to the melting of the bulk hydrocarbon regions of the lipids. (Journal abstract modified)

003859 Narasimhachari, N.; Friedel, R. O. Dept. of Psychiatry, Medical College of Virginia, Richmond, VA 23298 **GC-MS studies of phenelzine and its acyl derivatives.** Research Communications in Psychology, Psychiatry, and Behavior. 5(2):185-197, 1980.

The gas chromatographic and mass spectral (gcms) characteristics of trifluoroacetyl and acetyl derivatives of phenelzine were studied. Direct acetylation of phenelzine sulfate or hydrochloride with trifluoroacetic anhydride yields several products from which a mono and di TFA derivatives are identified by EI and CI gcms. Similarly acetic anhydride gives a mono and diacetyl derivatives characterized by EI and CI mass spectra. Alpha-phenylpropyl hydrazine which is used as an internal standard for quantitation of phenelzine also yields multiple derivates on acylation. 11 references. (Author abstract modified)

003860 Reifenrath, William G.; Roche, Edward B.; Al-Turk, Walid A.; Johnson, Howard L. Roche: Dept. of Biomedicinal Chemistry, College of Pharmacy, University of Nebraska Medical Center, Omaha, NE 68105 **Synthesis and biological activity of fluoroalkylamine derivatives of narcotic analgesics.** Journal of Medicinal Chemistry. 23(9):985-990, 1980.

The synthesis and biological activity of fluoroalkylamine derivatives of narcotic analgesics are described. N-ethyl-, N-(2-fluoroethyl)-, N-(2,2-difluoroethyl)-, and N-(2,2,2-trifluoroethyl) substituted normeperidine and normetazocine derivatives were prepared, and the analgesic activities of the compounds were determined in mice. Opiate receptor binding, in the presence and absence of sodium ion, was studied. The antagonist activities of normetazocine derivatives were studied in monkeys, and further examined in the isolated guinea-pig ileum for relative agonist activity. The pKa values were measured; in vivo agonist activity was lost with weakly basic derivatives. For the normetazocine derivatives, opiate receptor binding data were consistent with guinea-pig ileum agonist potency and mouse vas deferens antagonist potency but not with in vivo data. Opiate receptor binding was reduced for the less basic normetazocine derivatives. In the normeperidine series, there was no apparent direct relationship between pKa and opiate receptor binding. However, a relationship involving the hydrophobic character of the N-substitutent is discussed. The N-(2-fluoroethyl) derivatives in both series were found to cause convulsions in rats at doses of 40 to 45mg/kg ip. Elevated serum citrate levels were found in these rats, implicating in vivo oxidative deamination of the N-(fluoroalkyl) substitutent to fluoroacetate. (Author abstract modified)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

003861 Baldessarini, Ross J. Mailman Research Center, McLean Div. of Mass. Gen. Hospital Belmont, MA 02178 **Apomorphine prodrug derivatives as long-acting dopamine receptor active agents with potential clinical utility.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1596-1598).

Studies in rats of the in vivo and in vitro activities of a series of 0'0-diesters of apomorphine are described. The esters were somewhat less potent than apomorphine in inducing stereotyped

gnawing and rotational behavior and had a longer latency to maximal effect and a prolonged duration of action. Behavioral and biochemical studies suggest that the prolongation of action seen in the apomorphine derivatives may reflect depot properties of the esters or decreasing rates of hydrolysis to apomorphine, the active product. The potential use of apomorphine prodrugs in treating neurological, psychiatric, and neuroendocrinological disorders is discussed. 14 references.

003862 Dun, N. J.; Karczmar, A. G. Dept. of Pharmacology, Loyola University, Stritch School of Medicine, Maywood, IL 60153 **Blockade of ACh potentials by alpha-bungarotoxin in rat superior cervical ganglion cells.** Brain Research. 196(2):536-540, 1980.

The effects of alpha-bungarotoxin (alpha-BT) on the rat superior cervical ganglia were investigated. It was found that alpha-BT does not affect ganglionic transmission mediated by nicotinic receptors, but blocks completely or partially the membrane depolarization induced by iontophoresis of acetylcholine (ACh) or carbachol (Carb) onto the surface of ganglion cells. Furthermore, the receptor that was sensitive to the blockade of alpha-BT was also blocked by dihydro-beta-erythroidine or D-tubocurarine. These results suggest that alpha-BT sensitive receptors are present in mammalian sympathetic neurons and that they may represent extrajunctional ACh receptors. It is noted that alpha-BT may be a useful pharmacological tool for differentiating subpopulations among the nicotinic ACh receptors. 13 references.

003863 Glennon, Richard A.; Liebowitz, Stephen M.; Leming-Doot, Dianne. Dept. of Pharmaceutical Chemistry, School of Pharmacy, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Demethyl analogues of psychoactive methoxyphenalkylamines: synthesis and serotonin receptor affinities.** Journal of Medicinal Chemistry. 23(9):990-994, 1980.

Mono-O-demethylation of several, 2,5-dimethoxyphenalkylamines was found to increase their affinity for the serotonin receptors of the isolated rat fundus preparation. In several instances, demethylation of methoxyphenakylamines results in compounds which produce an antagonisms which is not of a competitive nature. With respect to 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM), demethylation of the 2-methoxy group alters affinity in a manner which parallels that observed upon demethylation of 5-methoxy-N,N-dimethyltryptamine. Using a discriminative stimulus paradigm, behavioral studies with rats reveal that the 2-hydroxy analogue, but not the 5-hydroxy analogue, of DOM produces effects (interoceptive cues) similar to those produced by 5-methoxy-N,N-dimethyltryptamine. (Author abstract)

003864 Hirai, K.; Ishiba, T.; Sugimoto, H.; Sasakura, K.; Fujishita, T.; Toyoda, T.; Tsukinoki, Y.; Joyama, H.; Hatakeyama, H. Shionogi Research Lab., Shionogi Co., Ltd., Fukushima-ku, Osaka 553, Japan **Peptidoaminobenzophenones, a novel class of ring-opened derivatives of 1,4-benzodiazepines.** Journal of Medicinal Chemistry. 23(7):764-773, 1980.

A series of novel peptidoaminobenzophenones has been prepared via several routes and is evaluated for CNS activity. The structure/activity relationships in the series are discussed. In general, dipeptido-N-methylaminobenzophenones showed higher activities than the corresponding NH derivatives. Some compounds had very high activities in antipentylenetetrazole and antifighting tests in mice when orally administered. Very weak toxicity was also found in these compounds. Water solubility of the peptidoaminobenzophenones and their salts was tested. Possible in vivo conversion of peptidoaminobenzophenone by enzymatic cleavage of the terminal amino acid, followed by chemical cyclization to 1,4-benzodiazepine, is also discussed. Such novel open ring derivatives of 1,4-benzodiazepine may serve as useful CNS agents. (Author abstract)

003865 Johnson, David N.; Turley, Brenda G.; Jones, Mary R.; Coffin, Cynthia B.; Leonard, C. A.; Funderburk, William H. Dept. of Pharmacology, A. H. Robins Research Laboratories, Richmond, VA 23220 **AHR-6646: a new, long-acting neuroleptic.** Progress in Neuro-Psychopharmacology. 3(5/6):513-520, 1979.

Preclinical, animal trials of AHR-6646, a new, long-acting neuroleptic are described. AHR-6646 blocked d-amphetamine lethality in mice under aggregated conditions when the pretreatment interval was between 1 hour and 7 days. Conditioned avoidance responding in mice and cats was suppressed by AHR-6646 in doses that did not impair escape behavior. The duration of this effect was markedly prolonged. AHR-6646 produced catalepsy in rats. The onset of this effect was delayed and the duration was prolonged when compared with that of chlorpromazine. Apomorphine-induced pivoting in mice with unilateral lesions of the caudate nucleus was suppressed by AHR-6646. AHR-6646 was a potent antiemetic agent in dogs, with a delayed onset and prolonged duration of action. 8 references. (Author abstract modified)

003866 Kovac, Tomislav; Kajfez, Franjo; Sunjic, Vitomir; Blazevic, Nikola; Kolbah, Dragutin. Chemical Research Company, H-6830 Chiasso, Corso San Gottardo 35, Switzerland **Synthesis of some carbon-3 substituted 1,4-benzodiazepin-2-ones and their central nervous system effects.** Journal of Medicinal Chemistry. 22(9):1093-1096, 1979.

Thirteen new carbon-3 substituted 1,4-benzodiazepin-2-ones were synthesized and tested for central activity in Swiss-Webster mice. Appreciable central activity was shown by beta-hydroxyethyl derivatives and their conjugates with acetylated sugar. Trichloroacetyl esters were also highly active, but showed high acute toxicity. Conjugates with glycerol were less active, and intermediary acetonides were inactive. No correlation between lipophilicity and CNS activity was observed. 21 references. (Author abstract modified)

003867 Mulder, Arie H.; Braakhuis, Boudewijn; de Regt, Victoria; Dijkstra, Durk; Horn, Alan S. Dept. of Pharmacology, Free University Medical Faculty, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands **Effects of ADTN and various other 2-aminotetralin derivatives on the efflux of 3H-dopamine from rat striatal slices.** European Journal of Pharmacology. 64(4):349-355, 1980.

The efflux of tritium from male Wistar rat striatal and hypothalamic slices labeled with 3H-dopamine was increased in a concentration dependent fashion by 2-amino-6,7-dihydroxytetralin (ADTN) and 2-amino-5,6-dihydroxytetralin (iso-ADTN), but iso-ADTN was less potent than ADTN. These effects were inhibited by cocaine and nomifensine. The phenol derivatives of 2-aminotetralin were less effective than the catechols, and 1-methyl-ADTN, 4-phenyl-ADTN, and the dimethoxy derivative of 2-aminotetraline were inactive. Of the mono and dihydroxy derivatives of N,N-dipropyl-2-aminotetralin, the 7-0H and 6,7-di0H compounds only slightly affected tritium efflux and the 6-0H, 5-0H, and 5,6-di0H compounds were inactive. 21 references. (Author abstract modified)

003868 O'Donnell, J. P.; Azzaro, A. J.; Urquilla, P. R. Dept. of Pharmacology, School of Medicine, West Virginia University Medical Center, Morgantown, WV 26506 **(3,4-Dihydroxybenzyl)-2-imidazoline (DHBI): an analogue of dopamine.** Research Communications in Chemical Pathology and Pharmacology. 26(2):243-251, 1979.

A phenethylamine congener of dopamine (DA), (3,4-dihydroxybenzyl)-2-imidazoline (DHBI) was prepared and tested for DA receptor activity. DHBI relaxed rabbit isolated renal and ear arteries in the presence of phenoxybenzamine and propranolol, whereas DA and the specific renal DA agonist 6,7-dihydroxy-2-aminotetrahydronaphthalene showed selective activity on the renal artery. DHBI failed to increase adenylate cyclase activity in the rat striatum, but did attenuate the stimulatory actions of DA on adenylate cyclase by about 50%. 18 references. (Author abstract modified)

003869 Rollema, Hans; Westerink, Ben H. C.; Mulder, Theo B. A.; Dijkstra, Durk; Feenstra, Matthijs G. P.; Horn, Alan S. Dept. of Medicinal Chemistry, Lab. for Pharmaceutical and Analytical Chemistry, Antonius Deusinglaan 2, 9713 AW Groningen, The Netherlands **The significance of COMT activity in controlling dopamine agonist levels in brain and serum: studies with a prodrug and a metabolite of 6,7-ADTN.** European Journal of Pharmacology. 64(4):313-323, 1980.

After i.p. administration of the dibenzoylesters of 2-amino-6,7-dihydroxytetralin (6,7-ADTN) and 2-amino-5,6-dihydroxytetralin (5,6-ADTN) to female Wistar rats, brain and serum concentrations of 6,7-ADTN were lower than those of 5,6-ADTN. These differences in concentration were due to differences in the compounds' susceptibility to catechol-0-methyltransferase (COMT). A substantial amount of 6,7-ADTN was converted by COMT to its metabolite 2-amino-6-hydroxy-7-methoxytetralin, which showed no dopaminergic activity in behavioral and biochemical tests. It is suggested that for certain catechols, high dopamine agonistic activity parallels increased susceptibility to COMT. 22 references. (Author abstract modified)

003870 Verimer, Turkiz; Long, John P.; Rusterholz, David R.; Flynn, Jan R.; Cannon, Joseph G.; Lee, Theresa. Dept. of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Dopaminergic activity of cis-trans isomers of benzhydro(f)quinoline analogs.** European Journal of Pharmacology. 64(4):271-277, 1980.

Experiments in several animal models showed that trans-isomers of 8,9-dihydroxy derivatives of octahydrobenzo(f)quinolines have potent central and peripheral dopaminergic activity. The cis-isomers were less active. Haloperidol antagonized the inhibitory effects exerted by all of these compounds except the N-methyl cis-isomer which was antagonized by phentolamine. The trans-tertiary compounds produced rotational behavior in rats and emesis in dogs; the cis-isomers were ineffective in both models. 17 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

003871 Allan, R. D.; Curtis, D. R.; Headley, P. M.; Johnston, G. A. R.; Kennedy, S. M. E.; Lodge, D.; Twitchin, B. Dept. of Pharmacology, University of Sydney, N.S.W., 2006, Australia **Cyclobutane analogs of GABA.** Neurochemical Research. 5(4):393-400, 1980.

Cis-3-aminocyclobutane-1-carboxylic acid and its trans-isomer were synthesized as conformationally restricted analogs of GABA. The cis-isomer displayed weak to moderate GABA-like activity in inhibiting GABA uptake in rat brain minislices, inhibiting sodium independent binding of GABA to rat brain membranes, acting as a substrate for GABA aminotransferase, and depressing the firing rate of cat spinal neurons. The trans-isomer was less effective in all four assays. It is suggested that the extra methylene group in trans-3-aminocyclobutane-1-caboxylic acid clips back the zwitterionic centers so that potent interaction with active sites for GABA is prevented by steric repulsion from the cyclobutane ring. 23 references. (Author abstract modified)

003872 Antov, G.; Kazakova, B.; Aynova, A. Institute of Hygiene and Occupational Health, Bulv. D. Nestorov 15, 1431 Sofia, Bulgaria **Warfarin-induced changes in activity of brain enzymes in rats.** Activitas Nervosa Superior. 21(4):278-279, 1979.

Changes in activity of brain enzymes in rats induced by ratron (warfarin), a rodenticide agent were examined. Ratron was administered orally in a water solution for 6 months to two groups of 20 male rats each, either 1/100 LD50 five times a week (group 1) or 1/50 LD50 intermittently (i.e., 1 week five doses, next week, no doses) (group 2). In group 1, a significant decrease of activity was found for ICDH and G6Pase. In group 2, significant decreases in ICDH, SucDH, GIDH, G6Pase, ATPase, ad CytO activity were found. Thiole groups were lower by 35%. Unequal distribution of enzymes in neurons, nervous fibers, brain membranes, and vascular walls were observed. 7 references.

003873 Aronstam, Robert S.; Eldefrawi, Amira T.; Eldefrawi, Mohyee E. Dept. of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD 21201 **Similarities in the binding sites of the muscarinic receptor and the ionic channel of the nicotinic receptor.** Biochemical Pharmacology. 29(9):1311-1314, 1980.

Similarities in the binding sites of the muscarinic receptor and the ionic channel of the nicotinic receptor were investigated in rats and in Torpedo ocellata electric organs. All 23 drugs tested inhibited competitively the specific binding of (3H)L-quinuclidinyl benzilate (3H)QNB to the muscarinic acetylcholine (ACh) receptor sites in membranes from rat brain cortex and tritiated perhydrohistrionicotoxin to sites on the ionic channel associated with the nicotinic ACh receptor in membranes from Torpedo electroplax. There are many similarities between the muscarinic receptors and nicotinic ionic channels, such as in their pharmacological specificities, in their possession of SH groups, alkylation of which inhibits ligand binding, and in their reaction to changes in pH, temperature, and ionic composition of the binding media. However, the many differences in their binding sites revealed in these results argue against a close molecular relationship. 11 references.

003874 Baez, L. A.; Browning, R. A.; Cusatis, M. Dept. of Psychology, Southern Illinois University, Carbondale, IL 62901 **Evaluation of body weight changes after selective serotonin depletion with 5,7-dihydroxytryptamine.** Progress in Neuro-Psychopharmacology. 4(2):123-127, 1980.

Treatment of rats with 5,7-dihydroxytryptamine (5,7-DHT) after pretreatment with protriptyline failed to produce any significant effect on bodyweight despite a marked depletion in forebrain serotonin (5-HT) an no effect on norepinephrine content. These findings conflict with previous reports in the literature suggesting marked enhancement in bodyweight following selective 5-HT depletion with 5,7-DHT and raise questions concerning the role of 5-HT in the regulation of bodyweight. Although the Ss used in this study were adults rather than juveniles, the failure to observe a bodyweight effect is not likely to be due to the age of the animal at time of treatment. Results do not support the hypothesis that serotonergic neurons exert a major influence in the regulation of growth and bodyweight. 21 references. (Author abstract modified)

003875 Baker, Walter W.; Kratky, Martha. Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA **Effects of cholinergic activation in the caudate on neuroregulation of motor, cortical, and hippocampal activities.** Psychopharmacological Bulletin. 16(2):27-29, 1980.

The effects of cholinergic activation in the caudate on neuroregulation of motor, cortical, and hippocampal activities are reviewed. Studies related to motor regulation have typically been performed in chronic cats, using a modified technique that permits the simultaneous recording of tremors and local brain electrographic activities following intracaudate microinjection of selective chemical agents. The importance of the critical balance between the excitatory effects of acetylcholine and the inhibitory actions of dopamine in the caudate as a basis for stabilizing motor functioning was demonstrated in a series of experiments. It is noted that intracaudate cholinergic and GABAergic mechanisms each altered the cortical somatosensory evoked potentials (SEP), but exerted completely opposite effects on the cortical response. 13 references.

003876 Baldino, Frank, Jr.; Beckman, Alexander L.; Adler, Martin W. CMDNJ-Rugers Medical School, Box 101, Piscataway, NJ 08854 **Actions of iontophoretically applied morphine on hypothalamic thermosensitive units.** Brain Research. 196(1):199-208, 1980.

The effects of iontophoretically applied morphine and naloxone were examined on 62 neurons in the preoptic/anterior hypothalamus (POAH) of urethane anesthetized Sprague-Dawley rats. Results demonstrate that morphine excited warm sensitive cells, which are assumed to mediate heat dissipation responses, and inhibit cold sensitive cells, which are assumed to mediate heat gain responses. These actions parallel morphine's hypothermic action in the intact animal and, therefore, suggest that morphine lowers body temperature by exerting a coherent action on POAH warm and cold sensitive neurons. Since these effects were antagonized by naloxone, the action of morphine on warm and cold sensitive cells seems to be mediated by an opiate receptor. 31 references. (Author abstract modified)

003877 Bannet, J.; Belmaker, R. H.; Ebstein, R. P. Ebstein: Jerusalem Mental Health Center-Ezrath Nashim, P.O.B. 140, Jerusalem, Israel **The effect of drug holidays in an animal model of tardive dyskinesia.** Psychopharmacology. 69(2):223-224, 1980.

The effect of drug holidays on the development of increased dopamine (DA) receptor binding in mouse caudate after haloperidol feeding was investigated, and the utility of this animal model for human tardive dyskinesia (TD) was assessed. Intermittent haloperidol treatment in mice increased 3H-spiroperidol binding to the same degree as continual haloperidol feeding. The absence of a positive effect of drug holiday on the molecular model of TD can serve to quell premature enthusiasm for drug holidays. Evidence for the similarity of this animal model to human TD is reviewed. 9 references. (Author abstract modified)

003878 Bearden, L. J.; Snead, O. C.; Healey, C. T.; Pegram, G. V. Neurosciences Program, University of Alabama in Birmingham, Birmingham, AL 35294 **Antagonism of gamma-hydroxybutyric acid-induced frequency shifts in the cortical EEG of rats by dipropylacetate.** Electroencephalography and Clinical Neurophysiology. 49(1-2):181-183, 1980.

An automated technique for the continuous analysis of selected EEG frequency bands as a function of drug treatment was employed to investigate the effects of dipropylacetate on gamma-hydroxybutyric acid (GHB)-induced frequency shifts in the cortical EEG of rats. Results show that the convulsive effects of GHB are antagonized by dipropylacetate, but that the effects of GHB exhibit a latent irreversibility. It is noted that both the onset of the hypersynchrony and the recovery from the electrical effects produced by GHB are easily observed by means of the frequency analysis technique used. This method permits the continuous analysis of selected frequency components of the EEG as a function of drug treatment, thus providing a quantitative assessment of the electrical effects of such agents. 20 references. (Author abstract modified)

003879 Bell, James A.; Sharpe, Lawrence G.; Berry, James N. NIDA, Division of Research, Addiction Research Center, Lexington, KY 40583 **Depressant and excitant effects of intraspinal microinjections of morphine and methionine-enkephalin in the cat.** Brain Research. 196(2):455-465, 1980.

The effects of intraspinal microinjections of morphine and methionine-enkephalin (Met-enkephalin) on the C-fiber and polysynaptic reflexes in the acute decerebrate low spinal cat were investigated. Microinjected into the dorsal horn, morphine and Met-enkephalin depressed the nociceptive C-fiber reflex without altering the short latency polysynaptic reflex. Microinjected into the ventral horn, morphine and Met-enkephalin facilitated the C-fiber and polysynaptic reflexes. Pretreatment of the cats with intravenous naltrexone antagonized the depressant effects produced by dorsal horn intrapinal microinjections of morphine and Met-enkephalin. The excitant effects of ventral horn microinjections of morphine were not antagonized by naltrexone. These results support a hypothesis that the analgesic effects of morphine at the spinal cord level are due to interactions with opiate receptors in the dorsal horn. 40 references (Author abstract modified)

003880 Ben-Barak, Jacob; Dudai, Yadin. Dept. of Neurobiology, Weizmann Institute of Science, Rehovot, Israel **Scopolamine induces an increase in muscarinic receptor level in rat hippocampus.** Brain Research. 193(1):309-313, 1980.

The effect of chronic administration of the muscarinic antagonist scoplamine on muscarinic receptors in the hippocampus of developing Wistar rats was examined. A significant supersensitivity, revealed by an increase in (3H)quinuclidinyl benzilate binding was detected as early postnatal day 4 and was more prominent by the second postnatal week. Supersensitivity was also observed in adult rats treated with scopolamine. 25 references.

003881 Bendek, Gyorgy; Hahn, Zoltan. Institute of Physiology, Szigeti u. 12, H-7643 Pecs, Hungary **Inhibition of 3H-thymidine incorporation into the DNA of developing rat brain by amphetamine treatment.** Progress in Neuro-Psychopharmacology. 3(5/6):555-558, 1979.

The inhibition of 3H-thymidine incorporation into the DNA of developing (10-day-old) rat brain by amphetamine treatment was investigated. The incorporation of labelled thymidine was decreased 2 hours after administration of 20 to 40mg/kg doses of amphetamine phosphate. The entry of precursor from the blood to the brain tissue was not disturbed. The observed elevation of plasma corticosterone levels did not appear to mediate the effect. Changes in the normal balance of tissue norepinephrine and dopamine levels are considered as possible inhibitory factors in glial cell proliferation. 11 references. (Author abstract modified)

003882 Bender, David A. Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, London W1P 7PN, England **Effects of benserazide, carbidopa and isoniazid administration on tryptophan-nicotinamide nucleotide metabolism in the rat.** Biochemical Pharmacology. 29(15):2099-2104, 1980.

The effects of benserazide, carbidopa, and isoniazid administration on tryptophan/nicotinamide nucleotide metabolism were investigated in rats. Weanling rats were maintained on a diet providing marginally adequate amounts of nicotinamide and vitamin B6, with a considerable excess of tryptophan to allow endogenous synthesis of nicotinamide nucleotides. Results confirm

to some extent the results obtained with benserazide, carbidopa, and isoniazid in vitro as inhibitors of the enzymes of tyrptophan oxidative metabolism in the rat, but show that pharmacokinetic factors are important, in that the apparent Ki values determined in vitro are not reflected in relative inhibitory potency following administration of the drugs. Results are discussed in relation to the mechanisms of isoniazid-induced pellagra and benserazide and carbidopa-induced niacin depletion in man. 18 references. (Author abstract modified)

003883 Benwell, Maureen E. M.; Balfour, D. J. K. Dept. of Pharmacology and Therapeutics, Dundee University Medical School, Ninewells Hospital, Dundee, Scotland **Effects of nicotine administration and its withdrawal on plasma corticosterone and brain 5-hydroxyindoles.** Psychopharmacology. 63(1):7-11, 1979.

The effects of nicotine administration and its withdrawal on the levels of brain hydroxyindoles and plasma corticosterone were studied in the rat. Daily injections of nicotine rapidly induced tolerance to the increase in plasma corticosterone seen in response to acute nicotine. Withdrawal of the drug from chronically treated animals caused a significant increase in plasma corticosterone. Hippocampal 5-hydroxytryptamine (5-HT) was reduced in nicotine treated rats, significantly so in those treated for more than 20 days. The changes in the hypothalamus and hippocampus appeared to be relatively specific since they differed from those seen in the rest of the brain. None of the effects could be related directly to changes in the plasma corticosterone concentration. 18 references. (Author abstract modified)

003884 Bergey, Gregory K.; martin, Michael R.; Hermes, Manfred. Dept. of Neurology, Johns Hopkins university School of Medicine Baltimore, MD 21205 **Effects of D,L-alpha-aminoadipate on postsynaptic amino acid responses in cultured mouse spinal cord neurons. agonists in the rat brain.** Brain Research. 193(1):19-207, 1980.

Intracellular recordings from mouse spinal cord neurons grown in dissociated cell culture were used to study the effects of the dicarboxylic amino acid, DL-alpha-aminoadipate (DLAA) on amino acid responses. Postsynaptic responses to iontophoretically applied aspartate were markedly antagonized by DLAA, but only slight antagonism to glutamate was observed. DLAA altered the affinity of aspartate for its receptor, but had no effects on aspartate/receptor cooperativity. DLAA had no direct effects on membrane potentials or passive membrane properties at current use for antagonism and did not alter responses to the inhibitory amino acids, glycine and GABA. 24 references. (Author abstract modified)

003885 Bhargava, Hemendra N. Dept. of Pharmacognosy and Pharmacology, College of Pharmacy, University of Illinois Medical Center, Chicago, IL 60612 **Enhanced sensitivity to pentobarbital in haloperidol or pimozide treated mice and rats.** Research Communications in Chemical Pathology and Pharmacology. 28(2):267-284, 1980.

The effect of haloperidol and pimozide (2.5 and 5.0mg/kg i.p.) on pentobarbital-induced narcosis, hypothermia, and lethality were studied in male Swiss-Webster mice and Sprague-Dawley rats. The neuroleptics increased the latency and duration of sleep induced by 60mg/kg sodium pentobarbital and enhanced the hypothermia response to 50mg/kg pentobarbital in rats; similar effects were seen in mice. Pimozide also significantly decreased the median lethal dose for pentobarbital in mice. Brain and plasma levels of pentobarbital on awakening were lower in rats treated with neuroleptics than in saline controls. 17 references. (Author abstract modified)

003886 Bhargava, Hemendra N. Dept. of Pharmacognosy and Pharmacology, University of Illinois at the Medical Center, Chicago, IL 60612 **Inability of cyclo (Leu-Gly) to facilitate the development of tolerance to and physical dependence on morphine in the rat.** Life Sciences. 27(12):1075-1081, 1980.

The effect of cyclo (Leu-Gly), an analog of melanotropin release inhibiting factor on the development of tolerance to and physical dependence on morphine in the rat was investigated. Administration of cyclo prior to and during morphine pellet implantation failed to facilitate the development of tolerance to the analgesic and hypothermic effects of morphine. Similarly, the development of dependence on morphine was not facilitated by cyclo, as evidenced by changes in body weight and body temperature observed during abrupt withdrawal of morphine. These studies do not lend support to the previous observations that cyclo and other related peptides facilitate the development of tolerance to and physical dependence on morphine. 13 references. (Author abstract)

003887 Biegon, Anat; Samuel, David. Dept. of Isotope Research, Weizmann Institute of Science, Rehovot, Israel **The in vivo distribution of an antidepressant drug (DMI) in male and female rats.** Psychopharmacology. 65(3):259-263, 1979.

The differences in the fate and in vivo distribution of desmethylimipramine (DMI) in male and female rats using the tritated drug, were investigated and the results were compared with those for the neuroleptic chlorpromazine (CPZ). Sex differences in response to DMI were found; these differences were not found when CPZ was administered. The pharmacokinetics and dose dependence of the accumulation of DMI were similar in males and females. The sex differences in the amount of DMI in brain, which may be the result of sex dependent metabolism in liver microsomes, may explain the male/female differences in reaction to antidepressants. 25 references. (Author abstract modified)

003888 Biegon, Anat; Yavin, Ziva; Yavin, Ephraim; Samuel, David. Dept. of Isotope Research, Weizmann Institute of Science, Rehovot, Israel **Characterization and ontogenesis of (3H)-desipramine binding sites in developing fetal rat cerebral cells in culture.** Biochemical Pharmacology. 29(12):1755-1757, 1980.

The characterization and ontogenesis of (3H)-desipramine binding sites in developing fetal rat cerebral cells in culture were investigated. The tricyclic antidepressant drug desipramine (DMI) was found to bind specifically to cultured cells from the fetal rat brain tissue in a saturable, displacable manner. The number of the binding sites is small during the first 48 h in culture and increases markedly from day 4 in a time dependent course which parallels early synaptogenesis. DMI binding is effectively inhibited following chronic treatment of the cultures with 6-hydroxydopamine (6-OHDA). The binding characteristics and the pharmacological profile of desipramine in developing cerebral cells are in excellent agreement with those found in adult rat brain. 13 references. (Author abstract modified)

003889 Birdsall, N. J. M.; Burgen, A. S. V.; Hulme, E. C.; Wells, J. W. Division of Molecular Pharmacology, National Institute for Medical Research, London NW7 1AA, England **The effects of ions on the binding of agonists and antagonists to muscarinic receptors.** British Journal of Pharmacology. 67(3):371-377, 1979.

The effects of ions on the binding of various agonists and antagonists to muscarinic receptors in rat brain were examined. Sodium, potassium, calcium, magnesium, and chloride ions showed no selective effects on the binding of agonists and antagonists, but a decrease in affinity related to ionic strength was observed for these ions. Larger effects were produced by thal-

lium and lanthanum ions and some transition metal ions. Results are discussed in relation to the bidirectional conformational coupling suggested for the morhpine receptor. 28 references. (Author abstract modified)

003890 Black, Asa C., Jr.; Sandquist, Dean; West, James R.; Wamsley, James K.; Williams, Terence H. Dept. of Anatomy, College of Medicine, University of Iowa, Iowa City, IA 52242 **Muscarinic cholinergic stimulation increases cyclic GMP levels in rat hippocampus.** Journal of Neurochemistry. 33(6):1165-1168, 1979.

The effects of muscarinic cholinergic stimulation on cyclic guanosine 3',5'-monophosphate (cGMP) levels in rat hippocampus were investigated via incubation of rat hippocampi with varying concentrations of bethanechol, a muscarinic cholinergic agonist. Increased levels of cGMP in rat hippocampi were found to be concentration dependent, with 500mcM bethanechol producing a maximum increase of 490% over control values. The bethanechol evoked increases were blocked by the muscarinic antagonist atropine, and were calcium dependent. It is concluded that at least some of the cells projecting to the rat hippocampus form muscarinic cholinergic synapses which act via a cGMP dependent mechanism. 33 references. (Author abstract modified)

003891 Bohmer, G.; Dinse, H. R. O.; Fallert, M.; Sommer, T. J. Dept. of Physiology, University of Mainz, D-6500 Mainz, Germany **Microelectrophoretic application of antagonists of putative neurotransmitters onto various types of bulbar respiratory neurons.** Archives Italiennes de Biologie. 117(1):13-22, 1979.

Seven antagonists of putative neurotransmitters were applied to rabbit bulbar respiratory neurons and also to nonspecific cells, and receptor properties of the various cell types were examined. With strychnine, specific antagonist of glycine, excitation prevailed in expiratory/inspiratory (EI), inspiratory (I), and expiratory (E) neurons. With bicuculline, about half of the nonspecific neurons were activated and the remainder were unresponsive. GDEE (glutamatediethylester), antagonist of glutamate, excited part of the inspiratory/expiratory (IE) neurons and inhibited part of the E units, while the remainder of both types as well as two EI cells tested were not affected. With flupentixol, antagonist of dopamine, about half of the IE and E units remained unaffected, while in the remainder E cells inhibition was dominant over excitation. With yohimbine, an alpha-adrenoceptor blocker, the two EI as well as the majority of the I neurons remained unaffected, with two cells of the latter type being activated. Propranolol, a beta-adrenoceptor blocker, inhibited about half of the E neurons while the remainder as well as most IE and the two EI cells tested were not affected. Cyproheptadin, an antagonist of 5-HT, excited most E neurons. As concerns NE receptors, those of the alpha type might be involved in activation of part of the E cells only, whereas all other NE effects (inhibition or activatiion) are mediated by CNS specific receptors different from the alpha and beta type. 5-HT effects apparently are mediated by two different receptor types. 20 references. (Author abstract modified)

003892 Bondy, Stephen C.; Tepper, James M.; Bettis, David B. National Institute of Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC 27709 **Seizure proneness and neurotransmitter uptake.** Neurochemical Research. 4(6):755-761, 1979.

The ability of midbrain homogenates from two strains of mice to accumulate several putative neurotransmitters, or their precursor in the case of acetylcholine, was examined. The high affinity transport mechanisms toward glutamate, GABA, dopamine, and glycine were similar in both strains. The seizure prone DBA/2IBG strain had a significantly higher capacity to transport choline than did the relatively seizure resistant C57BL/6IBG mice. However, no difference in the density of muscarinic binding sites in the two mouse strains was found. 24 references. (Author abstract)

003893 Braestrup, C.; Nielsen, M.; Nielsen, E. B.; Lyon, M. A/S Ferrosan, 5 Sydmarken, DK-2860 Soeborg, Denmark **Benzodiazepine receptors in the brain as affected by different experimental stresses: the changes are small and not undirectional.** Psychopharmacology. 65(3):273-277, 1979.

Rats and mice were exposed to several different stress situations to investigate whether brain benzodiazepine receptors were sensitive to altered external or internal environmental circumstances. Certain stresses resulted in small decreases in benzodiazepine receptor binding in some cerebral cortex of hippocampal areas while immobilization stress resulted in a small increase in frontal cortex. Other brain areas and other stresses (isolation of male mice, forced swimming, or chronic amphetamine intoxication) did not change receptor binding. It is concluded that the effect of prolonged stress on benzodiazepine receptors is complex and not very pronounced. 36 references. (Author abstract modified)

003894 Brookes, Neville; Burt, David R. Dept. of Pharmacology and Experimental Therapeutics, University of Maryland, School of Medicine, 660 W. Redwood St. Baltimore, MD 21201 **Development of muscarinic receptor binding in spinal cord cell cultures and its reduction by glutamic and kainic acids.** Developmental Neuroscience. 3(3):118-127, 1980.

The density of (3H)quinuclidinyl benzilate (3H-QNB) binding sites in dissociated cell cultures of mouse spinal cord increased almost fourfold between days 5 and 21 in vitro. Glutamate (0.1 to 1mM) caused a concentration dependent loss of 3H-QNB binding sites (up to 79%) and was only slightly less potent than kainic acid in this respect. The suceptibility of 8-day cultures to glutamate-induced loss of 3H-QNB binding sites was less than that of 12 and 19 day cultures. Results indicate that 80% or more of muscarinic binding sites in spinal cord cell cultures are on neurons, whose sensitivity to glutamate toxicity increases with maturation in vitro. 30 references. (Author abstract modified)

003895 Burki, Hans R. Research Institute Wander, a Sandoz Research Unit, Wander Ltd., P. O. Box 2747 Berne, Switzerland **Inhibition of 3H-clozapine binding in rat brain after oral administration of neuroleptics.** Life Sciences. 26(25):2187-2193, 1980.

The inhibition of 3H-clozapine binding in rat brain after oral administration of neuroleptics was investigated. Clozapine, thioridazine, perlapine, clothiapine, chlorpromazine, NT 104-252, loxapine, or haloperidol were administered orally, and atropine subcutaneously, to rats. The animals were decapitated, brain tissue was removed and homogenized in tris buffer and incubated with 3H-clozapine. Total and nonspecifically bound 3H-clozapine were measured in each preparation. A dose dependent inhibition of specific 3H-clozapine binding ofmore than 50% was observed only after the administration of clozapine or thioridazine. There was no correlation between inhibition of 3H-clozapine binding and that of 3H-haloperidol, a specific ligand for dopamine receptors. 3H-Clozapine receptor density was much greater than 3H-haloperidol receptor density, suggesting that the majority of clozapine binding sites are not dopamine receptors. 10 references. (Author abstract modified)

003896 Burnstein, Sumner; Hunter, Sheila A.; Sedor, Carolyn. Dept. of Biochemistry, University of Massachusetts, Medical School, Worcester, MA 01605 **Further studies on the inhibition**

of Leydig cell testosterone production by cannabinoids. Biochemical Pharmacology. 29(15):2153-2154, 1980.

The inhibition of Leydig cell testosterone production by cannabinoids was investigated. Cannabigerol showed the greatest potency in inhibiting testosterone synthesis, while cannabichromene was the least active with only about one tenth the potency. Delta1-tetrahydrocannabinol was among the least active substances tested. Results indicate that clinical studies involving steroid hormone levels should take into account the abundance of each of the cannabinoids in the drug samples used. Chronic exposure to cannabis could lead to appreciable levels of nonpsychoactive cannabinoids at steroidogenic sites in vivo. It is noted that some of the nonpsychoactive cannabinoids may be useful in therapeutic applications where a reduction in the synthesis of hormonally active steroids is desired, e.g., in the treatment of steroid dependent tumors. 8 references.

003897 Carr, Laurence A.; Wehry, Susan M. Dept. of Pharmacology and Toxicology, University of Louisville Health Sciences Center, Louisville, KY 40292 **Effect of cycloheximide and d-amphetamine on brain catecholamines in two mouse strains.** Pharmacology Biochemistry and Behavior. 13(2):193-197, 1980.

Cycloheximide caused a dose dependent inhibition of norepinephrine (NE) and dopamine (DA) synthesis in male C57BL/6J and DBA/2J mice. D-amphetamine partially prevented the decrease in the rate of synthesis of NE, DA, and normetanephrine caused by cycloheximide in the C57 strain, but enhanced the inhibition of synthesis of these compounds in the DBA strain. Results suggest that reported strain differences in sensitivity to the amnesic effects of cycloheximide may be associated with the degree of inhibition of catecholamine synthesis. 30 references. (Author abstract modified)

003898 Carter, R. B.; Leander, J. D. Dept. of Pharmacology, 1021 Fac. Lab. Office Bldg., 231H, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Evidence for a peripheral effect of serotonin or metabolites in 5-hydroxytryptophan-induced hypothermia.** Neuropharmacology. 19(8):777-784, 1980.

The hypothermia induced by 1-5-hydroxytryptophan (1-5-HTP, 25 to 200mg/kg i.p.) in male Sprague-Dawley rats was antagonized by pretreatment with benserazide, carbidopa, or xylamidine tosylate. Serotonin creatinine sulfate (5-HT, 5 to 20mg/kg i.p.) produced a dose dependent hypothermic effect similar to that of 1-5-HTP, and this effect was also blocked by xylamidine tosylate. Results suggest that the hypothermic effect of systemically administered 5-HTP in rats is due to actions of 5-HT or its metabolites outside the blood-brain barrier. 37 references. (Author abstract modified)

003899 Casamenti, Fiorella; Bianchi, Clementina; Beani, Lorenzo; Pepeu, Giancarlo. Dept. of Pharmacology, University of Florence, Viale Morgagni 65, I-50124 Florence, Italy **Effect of haloperidol and pimozide on acetylcholine output from the cerebral cortex in rats and guinea pigs.** European Journal of Pharmacology. 65(2/3):279-284, 1980.

The effects of haloperidol, pimozide, and amphetamine on acetylcholine (ACh) output from the cerebral cortex were studied in urethane anesthetized and unanesthetized male Wistar rats and guinea-pigs of both sexes. Haloperidol (1mg/kg i.p.) decreased ACh output only in the anesthetized rats and increased it only in unanesthetized guinea-pigs. Pimozide (1mg/kg i.p.) stimulated ACh in output in unanesthetized rats and guinea-pigs and anesthetized guinea-pigs, but not in anesthetized rats. Amphetamine (1mg/kg i.p.) stimulated ACh output in all groups. In rats with a septal lesion, the effect of amphetamine on ACh output was suppressed, but that of pimozide persisted. 21 references. (Author abstract modified)

003900 Casamenti, Fiorella; Pedata, Felicita; Corradetti, R.; Pepeu, G. Dept. of Pharmacology, University of Florence, Viale Morgagni 65, I-50134 Florence, Italy **Acetylcholine output from the cerebral cortex, choline uptake and muscarinic receptors in morphine-dependent, freely-moving rats.** Neuropharmacology. 19(7):597-605, 1980.

Spontaneous acetylcholine (ACh) output from the cerebral cortex did not differ from control levels in morphine dependent male Wistar rats, but increased 60% during naloxone precipitated withdrawal. In rats made dependent after a large septal lesion or treated for 10 days with calcium gluconate, no increase in ACh output was observed during withdrawal. Choline high affinity uptake in the cerebral cortex and caudate nucleus showed a marked increase during withdrawal. The affinity of muscarinic receptors for tritiated quinuclidinyl benzilate was significantly increased in the cerebral cortex and caudate nucleus of morphine dependent rats, but returned to normal during naloxone precipitated withdrawal. In the caudate nucleus, the number of binding sites was decreased before and after the withdrawal syndrome. 34 references. (Author abstract modified)

003901 Chan, Pak H.; Fishman, Robert A.; Lee, Janie L.; Candelise, Livia. Brain Edema Clinical Research Center, Dept. of Neurology, University of California, San Francisco, CA 94143 **Effects of excitatory neurotransmitter amino acids on swelling of rat brain cortical slices.** Journal of Neurochemistry. 33(6):1309-1315, 1979.

With the single rat brain cortical slice serving as in vitro bioassay system, the effects of neurotransmitter amino acids (1mN) on brain swelling, water, sodium and potassium content, inulin space, and lactate production were studied. The putative dicarboxylic amino acid neurotransmitters, L-glutamic acid and L-aspartic acids, greatly increased intracellular brain swelling with increased intracellular Na, water content, and lactate production, and decreases inulin space and intracellular K. Equimolar GABA, taurine, glycine, the putative inhibitory neurotransmitter amino acids, and equimolar alpha-amino-isobutyric acid had no effect. Brain swelling and intracellular Na/K rations were greatly increased by L-glutamate and L-aspartate at a concentration of 10mM. However, L-aspartate at these concentrations greatly depleted the K content and lactate production as compared to L-glutamate. Further studies indicated that only the structural analogs and isomers of the dicarboxylic amino acids possessing two acidic groups and an alpha-amino group had a similar effect on the induction of brain swelling. Among the analogs of glutamic acid, DL-homocysteic acid and kainic acid had a greater effect on brain swelling, as observed from the total adenosine 5'-triphosphate (ATP) levels and the time course and dose response. A biphasic response in lactate production was induced by DL-homocysteic acid and kainic acid, suggesting that these analogs had a neurotoxic effect on cellular metabolism at higher concentrations. 19 references. (Author abstract modified)

003902 Chandra, Satya V.; Shukla, Girja S.; Saxena, D. K. Industrial Toxicology Research Centre, Lucknow, Uttar Pradesh, India **Manganese-induced behavioral dysfunction and its neurochemical mechanism in growing mice.** Journal of Neurochemistry. 33(6):1217-1221, 1979.

Manganese-induced behavioral dysfunction and its neurochemical mechanism in growing mice were investigated. Suckling mice were exposed to manganese from birth indirectly, via their mothers, and then directly through drinking water after weaning. The growth and development of these mice and their age

matched controls were almost identical. Motor activity of offspring measured at 30 day intervals showed a significant increase at 60 and 90 days in manganese treated mice compared to controls. Increased motor activity was associated with significant elevation in the levels of dopamine and norepinephrine in the corpus striatum of treated mice. The levels of striatal tyrosine, homovanillic acid and manganese were also significantly increased in mice after manganese exposure. Thus, an animal model of early manganese poisoning has been developed with a possible role of striatal amines in the production of behavioral dysfunction in the treated mice. Implications of these findings are discussed in relation to the manifestations of the psychiatric phase of early manganese poisoning in humans. 20 references. (Author abstract modified)

003903 Chiueh, C. C.; Thoa, N. B. Laboratory of Neurosciences, NIA, Gerontology Research Center, Baltimore City Hospitals, Baltimore, MD 21224 **Turnover of hypothalamic catecholamines in spontaneously hypertensive rats.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1455-1457).

After alpha-methyltyrosine (aMT), depletion of norepinephrine (NE) and dopamine (DA) in the hypothalamus (but not brainstem) of 1 and 10-month-old spontaneously hypertensive rats (SHR) was greater than that in their Wistar-Kyoto controls. Immobilization enhanced the rate of depletion of NE and DA, but not of epinephrine (EPI), in brain. The aMT treatment produced a greater decrease in catecholamines in the hypothalamus and frontal cortex of immobilized adult SHR than in young SHR. Clonidine caused a decrease in brain NE turnover and an increase in EPI turnover. These results suggest that immobilization stress can produce hyperreactivity in the adrenergic systems in the hypothalamus and frontal cortex of SHR. 6 references. (Author abstract modified)

003904 Cho, C. H.; Pfeiffer, C. J.; Cheema, A. Dept. of Zoology, University of Toronto, 25 Harbord St., Toronto, Ontario M5S 1A1, Canada **Studies of zinc and histamine on lysosomal fragility: possible role in stress ulceration.** Pharmacology Biochemistry and Behavior. 13(1):41-44, 1980.

Zinc sulfate protected male Wistar rats against gastric ulceration induced by cold water immersion/restraint and reduced the associated increase in beta-glucuronidase release in the gastric mucosa. Zinc also reduced the release of this enzyme in isolated hepatic lysosomes in vitro, whereas histamine, an ulcer enhancing agent, had the opposite effect. Results suggest that zinc may protect against stress ulceration by stabilizing the lysosomal membrane. 18 references. (Author abstract modified)

003905 Clark, Wesley G.; Clark, Yvonne L. Dept. of Pharmacology, Southwestern Medical School, University of Texas Health Science Center, Dallas, TX 75235 **Changes in body temperature after administration of acetylcholine, histamine, morphine, prostaglandins and related agents.** Neuroscience and Biobehavioral Reviews. 4(2):175-240, 1980.

The literature on thermoregulatory effects of cholinergic agonists and antagonists, histamine and H1 and H2 receptor antagonists, narcotic analgesics and antagonists, prostaglandins, and related agents is reviewed. The tabulations include the species used, route or administration and dose of drug, ambient temperature, number of tests, and direction and magnitude of body temperature change. Special conditions, such as age, lesions, drug dependence, and drug interactions, are included. 572 references. (Author abstract modified)

003906 Clark, Wesley G.; Ponder, Stephen W. Dept. of Pharmacology, Southwestern Medical School, University of Texas Health Science Center, Dallas, TX 75235 **Thermoregulatory effects of (D-ala2)-methionine-enkephalinamide in the cat. Evidence for multiple naloxone-sensitive opioid receptors.** Brain Research Bulletin. 5(4):415-420, 1980.

At an ambient temperature of 22 degrees C, injection of (D-ala2)-methionine-enkephalinamide (DAME) into the third ventricle of cats caused dose related hyperthermias in the dose range of 3.1 to 5.0mcg. Larger doses were less effective and occasionally produced hypothermia. A 12.5mcg dose of DAME caused hyperthermia at ambient temperatures of 4 and 32 degrees, whereas a 200mcg dose induced hyperthermia at 22 and 32 degrees but usually caused hypothermia at 4 degrees. Responses to DAME were antagonized by naloxone. Central injection of beta-endorphin (5 to 50mcg) caused dose related hyperthemia. (Des-tyrl)-enkephalin (10 to 250mcg) was weakly hyperthermogenic and kytorphin (500mcg) did not consistently alter body temperature. 13 references. (Author abstract modified)

003907 Clarke, G. D.; Ryan, P. J. Cell Proliferation Laboratory, Imperial Cancer Research Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England **Tranquillizers can block mitogenesis in 3T3 cells and induce differentiation in Friend cells.** Nature. 287(5778):160-161, 1980.

The findings that benzodiazepines can block mitogenesis in 3T3 cells and induce differentiation in Friend cells are reported, and implications for cancer chemotherapy are discussed. Murine Friend erythroleukemia (MEL) cells were incubated for 5 days with concentrations of eight benzodiazepines and were stained with benzidine reagent to determine the proportion of the cell population which had accumulated hemoglobin. The effects of these eight benzodiazepines in blocking mitogenesis in 3T3 incubated cells were also investigated. Induction of differentiation by two tranquillizers supports the view that lipophilic drugs and inducers are a single group, active by virtue of membrane solubility. The finding that five known inducers and now diazepam, inhibit 3T3 cells at concentrations at which they induce differentiation in Friend cells, is compatible with a hypothetical inverse relationship between the probabilities of proliferation and terminal differentiation.

003908 Clements-Jewery, S.; Robson, P. A. Biochemical Pharmacology Section, Biological Research Dept., Roussel Laboratories Ltd., Swindon, Wiltshire, England **The in vivo and in vitro occupation of (3H)-spiperone binding sites in the frontal cortex and striatum by putative 5-hydroxytryptamine antagonists.** Neuropharmacology. 19(7):657-661, 1980.

The influence of putative serotonin (5-HT) antagonists and other psychotropic drugs on (3H)-spiperone binding in the frontal cortex and striatum were studied in vitro in rats and in vivo in mice. Results revealed a heterogeneity of binding sites, suggesting that (3H)-spiperone labeled both 5-HT and dopamine (DA) receptors in vivo and in vitro. Some antidepressant agents selectively occupied binding sites in the frontal cortex. Cataleptogenic neuroleptic drugs were more active at striatal dopaminergic sites, but the noncataleptogenic agent clozapine showed preferential activity at 5-HT receptors in the frontal cortex. 14 references. (Author abstract modified)

003909 Clow, Angela; Theodorou, Andreas; Jenner, Peter; Marsden, C. David. Marsden: King's College Hospital Medical School, Denmark Hill, London, SE5, England **Changes in rat striatal dopamine turnover and receptor activity during one years neuroleptic administration.** European Journal of Pharmacology. 63(2/3):135-144, 1980.

In male Wistar rats treated orally with trifluoperazine (2.5 to 3.5mg/kg/day) or thioridazine (30 to 40mg/kg/day) for up to 1 year, homovanillic acid and 3,4-dihydroxyphenylacetic acid

concentrations in the striatum increased initially but returned to normal within 1 month. Dopamine concentrations were elevated after 3 month treatment with either drug and after 12 month treatment with trifluoperazine. Trifluoperazine treatment for 1 month produced a marked increase in the dissociation constant (Kd) for striatal 3H-spiperone binding and a reduction in receptor numbers. However, receptor numbers were increase at 6 and 12 months in both drug groups. The Kd returned to normal at 6 months in both groups, but was elevated again at 12 months. Dopamine stimulation of striatal adenylate cyclase was inhibited by trifluoperazine or thioridazine administration for 1 week or 1 month, but this effect was replaced by enhanced stimulation after 6 or 12 months of drug treatment. 19 references. (Author abstract modified)

003910 Clow, Angela; Theodorou, Andreas; Jenner, Peter; Marsden, C. David. Marsden: King's College Hospital Medical School, Denmark Hill, London, SE5, England **Cerebral dopamine function in rats following withdrawal from one year of continuous neuroleptic administration.** European Journal of Pharmacology. 63(2/3):145-157, 1980.

Withdrawal responses were studied in male Wistar rats treated continuously with trifluoperazine (2.5 to 3.5mg/kg/day) or thioridazine (30 to 40mg/kg/day) for 1 year. Spontaneous locomotor activity increased 2 weeks after rug withdrawal. The enhanced steriotypic response to apomorphine seen during neuroleptic treatment persisted for up to a month after withdrawal, but spontaneous mouthing disappeared within 2 weeks. The increase in maximum binding capacity for 3 months after withdrawal, elevated dissociation constant returned to normal within 2 weeks of withdrawal. Dopamine stimulation of striatal adenylate cyclase remained enhanced 6 months after withdrawal. 26 references. (Author abstract modified)

003911 Collins, Robert C.; McLean, Mary; Olney, John. Dept. of Neurology, Box 8111, Washington University Medical School, 660 S. Euclid, St. Louis, MO 63110 **Cerebral metabolic response to systemic kainic acid: 14C-deoxyglucose studies.** Life Sciences. 27(10):855-862, 1980.

Glucose utilization and behavior were studied in Sprague-Dawley rats treated with kainic acid (KA, 12mg/kg i.v.). Staring spells were followed by wet dog shakes and overt convulsions within 90 minutes of injection; the convulsions lasted up to 18 hours and were followed by aphagia, adipsia, and startle behavior. Deoxyglucose autoradiography revealed a three to six-fold increase in glucose utilization in the ventral CA3 hippocampus, ventral subiculum, and lateral septum and a less intense increase in dorsal hippocampus 5 minutes after KA. During severe convulsions, the entire limbic system and its subcortical projections were metabolically active, while sensory pathways and neocortex were depressed. Many limbic areas involved in the seizures were necrotic 1 to 3 days after convulsions, when metabolism in the rest of the brain had returned to normal. 22 references. (Author abstract modified)

003912 Cordova, Tova; Ayalon, Daniel; Lander, Naftali; Mechoulam, Raphael; Nir, Isaac; Puder, Moshe; Lindner, Hans R. Dept. of Hormone Research, Weizmann Institute of Science, Rehovot, Israel **The ovulation blocking effect of cannabinoids: structure-activity relationships.** Psychoneuroendocrinology. 5(1):53-62, 1980.

Various cannabinoid compounds were tested for ovulation blocking in rats, and the possibility of separating hormonal actions from psychotropic ones was investigated. When administered at 14:00 hr on the preestrous day, delta-1-tetrahydrocannabinol (delta-1-THC) prevented ovulation, while delta-6-THC was a less potent inhibitor of ovulation. However, the 5'-(1●,2●dimethylheptyl) (DMH) homologue of delta-6-THC was 60 times more potent at ovulation blocking than the parent compound and 15 times more potent than delta-1-THC. ()Cannabidiol (()-CBD) was only weakly active, and two other cannabinoids were inactive, but the substitution of a DMH side chain for the amyl side chain of these three compounds significantly enhanced ovulation inhibiting activity. ()CBD-DMH, which inhibited ovulation in the rat, was found to be devoid of psychotropic activity when tested in rhesus monkeys. Thus, it appears that a separation of psychotropic and hormonal activity in the cannabinoids is possible. 25 references. (Author abstract modified)

003913 Coult, D. B.; Howells, D. J. Biology Division, Chemical Defence Establishment, Porton Down, Wiltshire, SP4 OJQ, England **Adenylate and guanylate cyclases in the cerebellum.** Biochemical Pharmacology. 28(17):2673-2675, 1979.

The effects of GABA, acetylcholine (ACh), putative GABA antagonists, and anticovulsants on adenylate and guanylate cyclase activities in male Wistar rat cerebellar homogenates were examined. Results provide evidence for activation of adenylate cyclase by GABA and of guanylate cyclase by ACh. GABA antagonists such as picrotoxin and N-methyl bicuculline inhibited the GABA activation of adenylate cyclase. Convulsants had no obvious effect on the basal rate of the enzyme, and anticonvulsants had no effect on the activation by GABA. None of the compounds altered the basal or ACh activated rate of guanylate cyclase. 12 references.

003914 Crunelli, V.; Bernasconi, S.; Samanin, R. Samanin: Istituto di Ricerche Farmacologiche Negri,' Via Eritrea, 62 I-20157 Milan, Italy **Evidence against serotonin involvement in the tonic component of electrically-induced convulsions and in carbamazepine anticonvulsant activity.** Psychopharmacology. 66(1):79-85, 1979.

Serotonin involvement in the tonic component of electrically-induced convulsions and in carbamazepine anticonvulsant activity was investigated. Intraventricular injection of 5,7-dihydorxytryptamine, selective destruction of descending serotonergic neurons by 5,6-dihydroxytryptamine, or electrolytic and chemical lesions of the nucleus raphe dorsalis did not affect the electroconvulsive threshold in rats. No effect was observed after the systemic administration of drugs known to increase central serotonin transmission, such as quipazine, m-chlorophenyl-piperazine, and moderate doses of d-fenfluramine; whereas p-chlorophenylalanine, an inhibitor of serotonin synthesis, decreased seizure susceptibility. The anticonvulsant activity of carbamazepine was not modified in animals with the same experimental lesions. Results, in relation to the high selectivity of the experimental procedures employed to deplete brain and spinal cord serotonin, do not bear out any involvement of serotonin in the tonic component of electrically-induced convulsions or in the action of carbamazepine. 55 references. (Author abstract modified)

003915 Dafny, N.; Gonzalez, L. P.; Altshuler, H. L. Dept. of Neurobiology and Anatomy, University of Texas, Health Science Center, P.O.B. 20708, Houston, TX 77025 **Effects of cocaine on sensory evoked potentials recorded from hypothalamus and limbic structures.** Progress in Neuro-Psychopharmacology. 3(4):353-360, 1979.

The effects of cocaine on sensory evoked responses were examined in freely moving male Sprague-Dawley rats. Results showed that each structure and each component of the average sensory evoked potentials were affected differently by the drug. In general, lower doses (0.25 or 0.5mg/kg) induced an increase in the sensory amplitude response, whereas the highest dose

(10.0mg/kg) resulted in attenuation of sensory responses. It is suggested that the euphoric effect of cocaine is due to potentiation of sensory input within the limbic/hypothalamic system; fatality induced large doses of the drug may be due to depression of sensory input. 15 references. (Author abstract modified)

003916 Davis, A.; Poat, J. A.; Woodruff, G. N. Dept. of Physiology and Pharmacology, Southampton University, Southampton, England **The use of R()-ADTN in dopamine receptor binding assays.** European Journal of Pharmacology. 63(2/3):237-238, 1980.

The specific binding of tritiated 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (ADTN) to purified rat striatal membranes was potently inhibited by dopamine agonists and antagonists. The system showed a high degree of stereospecificity; R()-ADTN was 300 times more potent than S(-)-ADTN, ()-butaclamol was 450 times more potent than (-)-butaclamol, and cis-flupenthixol was more potent than trans-flupenthixol in displacing 3H-ADTN binding. Haloperidol showed only weak activity. Results suggest that agonists and antagonists may bind with similar affinity to postsynaptic dopamine receptors. 5 references.

003917 DeFeudis, F. V.; Ossola, L.; Mandel, P. Centre de Neurochimie du CNRS, Faculte de Medecine, F-67085 Strasbourg Cedex, France **More muscimol binding sites than GABA binding sites in a particulate fraction of rat brain.** Biochemical Pharmacology. 28(17):2687-2689, 1979.

The binding capacities of muscimol and GABA were compared in a particulated fraction of male Wistar rat brain. The affinity of the particles for(3H)muscimol was about three times greater than that for (3H)GABA, and the maximum binding capacity of (3H)muscimol was about twice that of (3H)GABA. Results indicate that (3H) muscimol binds not only to GABA receptors but also to other sites in the particulate fraction. 13 references.

003918 DeFrance, Jon F.; Stanley, J. C.; Taber, K. H.; Marchand, J. E.; Dafny, N. Dept. of Neurobiology, University of Texas Medical School, Houston, TX 77025 **Effect of morphine on the excitability of rabbit hippocampus.** Experimental Neurology. 69(2):311-317, 1980.

The effects of morphine with respect to the excitability of hippocampal pyramidal cells were studied in acutely prepared rabbits. Microelectrode techniques were used for stimulation, recording, and iontophoresis of morphine and naloxone. Field potential responses were recorded before, during, and after drug delivery in different hippocampal layers. The data indicate that morphine administration results in a naloxone reversible enhancement in pyramidal cell excitability. Supersensitivity was seen with repeated, but short-term, administration of morphine. 21 references. (Author abstract)

003919 Desarmenien, Michel; Lamour, Yvon; Feltz, Paul. Laboratoire de Physiologie et Chimie Biologie U. L. P., 21 rue Rene-Descartes, F-67000 Strasbourg, France **Effects of diazepam on GABA-evoked depolarization in rat dorsal root ganglia in vivo.** Progress in Neuro-Psychopharmacology. 4(1):31-36, 1980.

The effects of benzodiazepines on a GABA sensitive membrane were assessed via intracellular recordings in dorsal root ganglion neurons. Diazepam had no effect on neuronal resting potential, membrane conductance, or excitability. Interactions with GABA-induced depolarization were studied: no clear antagonism or potentiation was observed. The rate of decay of GABA responses was accelerated, however, resulting in an apparent reduction of desensitization. Diazepam thus has no direct GABA-like action on this system, but there are nonetheless complex interactions between the two compounds, indicating a site of action on the GABA sensitive membrane. 19 references. (Author abstract modified)

003920 Dishovski, H.; Ivanova-Chemishanska, L. Institute of Hygiene and Occupational Health, Bulv. D. Nestorov 15, 1431 Sofia, Bulgaria **Ultrastructural changes in the neocortex of rats after chronic dithiocarbamate Antracol.** Activitas Nervosa Superior. 21(4):279-280, 1979.

Ultrastructural changes in the neocortex of rats after chronic dithiocarbamate (Antracol) were studied. Albino rats received either 1/100 LD50 (group 1 or 1/20 LD50 (group 2) for 40 days, and samples of sensorimotor cortex were examined via electron microscopy. Ultrastructure changes were intensive in group 2, affecting pyramidal cells primarily. The granulated endoplasmatic reticulum was strongly developed, and sometimes several long parallel cisterns covered with ribosomes or enlarged cisterns were observed. Results suggest certain functional pressure on the neuronal elements, accompanied probably by a rise in the synthetic processes.

003921 Divakaran, P.; Rigor, B. M.; Wiggins, R. C. Wiggins: Dept. of Neurobiology and Anatomy, University of Texas Medical School at Houston, P.O. Box 20708, Houston, TX 77025 **Brain cyclic nucleotide responses to anesthesia with halothane delivered in air or purified oxygen.** Journal of Neurochemistry. 35(2):514-516, 1980.

Brain cyclic nucleotide responses to anesthesia with halothane delivered in air or purified oxygen were investigated. Inhalation of either 0.5% or 1.0% halothane in air caused a slight decrease in the cyclic AMP concentration in rat cerebral cortex and cerebellum. During recovery, concentrations returned to normal in 3 h or less. In contrast, cyclic GMP decreased sixfold in cerebellum, but increased twofold in cortex. Recovery time for cerebellum was several hours. When oxygen was used as the carrier gas for halothane delivery, cAMP in the cortex doubled, in striking contrast to the case with halothane in air. Oxygen alone had no apparent effect. The cyclic GMP effect of halothane delivered in oxygen appeared the same as for halothane in air. Thus, the cyclic AMP effects of brain halothane are related to the enrichment of oxygen. 11 references. (Author abstract modified)

003922 Dobson, Robin A.; Johnson, W. E. Colleges of Pharmacy, Idaho State University, Pocatello, ID **Effects of general central nervous system depressants with and without calcium ionophore A23187 on rat cerebellar cyclic guanosine 3′,5′-monophosphate.** Research Communications in Chemical Pathology and Pharmacology. 29(2):265-280, 1980.

Cyclic guanosine monophosphate (cGMP) concentrations in male Sprague-Dawley rat cerebellum were reduced by ethanol, pentobarbital sodium, or diethyl ether. The calcium ionophore A23187 significantly increased cGMP levels when given alone, but depressed cGMP levels in animals acutely intoxicated with ethanol, pentobarbital, or diethyl ether. Results suggest the effects of the CNS depressants on cGMP were due to actions on calcium membrane sites, calcium influx, or intracellular calcium storage. 42 references. (Author abstract modified)

003923 Doherty, John D.; Simonovic, Miljana; So, Rebecca; Meltzer, Herbert Y. Dept. of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL 60637 **The effect of phencyclidine on dopamine synthesis and metabolism in rat striatum.** European Journal of Pharmacology. 65(2/3):139-149, 1980.

Phencyclidine (PCP, 2.5 to 50mg/kg i.p.) decreased the rate of accumulation of 3,4-dihydroxyphenylalanine (DOPA) in the striatum of male Sprague-Dawley rats, but did not antagonize the increases in DOPA accumulation induced by haloperidol,

reserpine, or gamma-butyrolactone. PCP decreased striatal levels of 3,4-dihydroxyphenylacetic acid and homovanillic acid when given alone, but potentiated the haloperidol-induced increases in striatal levels of these metabolites. PCP was not as effective as amphetamine in promoting the release of labeled dopamine (DA) from preloaded striatal slices in vitro. Results suggest that PCP potentiates the synaptic effects of endogenous DA and has a mechanism of action similar to that of the nonamphetamine stimulants (methylphenidate, amfonelic acid, and cocaine). 69 references. (Author abstract modified)

003924 Donelson, Alan C.; Bosin, Talmage R.; Campaigne, Ernest; Rogers, Richard B.; Maickel, Roger P. Section on Pharmacology, Medical Sciences Program, Indiana University, Bloomington, IN 47401 **Comparative effects of 5,6-dihydroxytryptamine and its benzo(b)-thiophene analogue on biogenic amines in the rat.** Biochemical Pharmacology. 28(22):3339-3343, 1979.

The effects of 5,6-dihydroxytryptamine (5,6-DHT) and its benzo(b)thiophene analogue on tissue levels of serotonin (5-HT) and norepinephrine (NE) in male Sprague-Dawley rats were compared. After intraperitoneal administration, both compounds significantly reduced NE levels in heart and spleen, but only 5,6-DHT reduced spleen 5-HT. Neither compound had any effect on brain NE or 5-HT after i.p. administration. When injected directly into the lateral ventricle, both compounds reduced NE levels, but the effect lasted less than 1 day. A prolonged reduction in brain 5-HT and 5-hydroxyindoleacetic acid levels was observed after 5,6-DHT, but the benzo(b)thiophene analogue had no effect. 24 references. (Author abstract modified)

003925 Dostalova, K.; Hrbek, Jan. Dr. S. Allende 3, 775 15 Olomouc, Czechoslovakia **Paradoxical sleep deprivation influenced by pyrithioxine.** Activitas Nervosa Superior. 22(2):113-114, 1980.

The influence of pyrithioxine on the changes in free ammonia level in various structrures of the central nervous tissue system (cortex, cerebellum hypothalamus, and brainstem) following paradoxical sleep deprivation in rats was investigated. Pyrithioxine was chronically administered for 10 days (6 days prior to the stress and 4 days during paradoxical sleep deprivation) in drinking water. Chronic administration of pyrithioxine produced a statistically significant decrease in ammonia production in cerebral cortex and brainstem. However, there was a significant acceleration in the return of free ammonia as early as after 3 hours of restitution sleep. 3 references

003926 Duka, Theodora; Wuster, Michael; Herz, Albert. Abt. fur Neuropharmakologie, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Rapid changes in enkephalin levels in rat striatum and hypothalamus induced by diazepam.** Naunyn-Schmiedeberg's Archives of Pharmacology. 309(1):1-5, 1979.

Acute treatment with diazepam (2.5mg/kg i.v.) resulted in pronounced changes in brain enkephalin concentrations in male Sprague-Dawley rats. Diazepam increased enkephal in concentrations in the hypothalamus by about 35%, lowered it in the corpus striatum by about 25%, and did not alter concentrations in the medulla oblongata/pons or midbrain. The onset of the drug-induced changes was rapid, with peak effects 2 to 5 minutes after injection. Enkephalin concentration in the hypothalamus returned to normal within 20 minutes, but the decrease in the striatum lasted for more than 60 minutes. The increased enkephalin concentration in the hypothalamus may be related to the antistress effect of the benzodiazpines, but the decrease in striatal enkephalin has no obvious behavioral correlate. 31 references. (Author abstract modified)

003927 Eckernas, Sven-Ake; Sahlstrom, Lena; Aquilonius, Sten-Magnus. Dept. of Neurology, University of Uppsala, Uppsala, Sweden **Effects of atropine treatment on cortical, striatal and hippocampal high-affinity uptake of choline in the mouse.** Life Sciences. 27(8):641-645, 1980.

Changes in high affinity uptake of choline (HACh) were studied in synaptosomes from different mouse brain regions following intravenous administration of atropine in vivo. The Ch uptake was expressed as a Ch uptake index, defined as the ratio between HACh and the corresponding choline acetyltransferase (ChAT) activity. The Ch uptake index was highest in the hippocampus and lowest in the striatum. In the hippocampus, a dose dependent increase in this index was found following atropine treatment, while the striatal Ch uptake index was unaffected by atropine. Atropine given i.v. in a dose of 10mg/kg induced on 86% increase in Vmax in synaptosomes from the hippocampus. 11 references. (Author abstract)

003928 Ellis, John; Hoss, Wayne. Center for Brain Research, School of Medicine and Dentistry, University of Rochester, Rochester, NY 14642 **Analysis of regional variations in the affinities of muscarinic agonists in the rat brain.** Brain Research. 193(1):189-198, 1980.

The brainstem of male Sprague-Dawley rats showed higher affinity for muscarinic agonists than did the forebrain. Binding characteristics in the two regions suggested the presence of two noninteracting binding sites. Analysis of the binding of the antagonist (3H)quinuclidinyl benzilate in the presence of carbachol indicated that brainstem and forebrain regions differ in dissociation constants for high affinity and low affinity receptors. It is suggested that whole brain contains at least three major muscarinic receptors, which can be distinguished on the basis of their affinities for agonists. 22 references. (Author abstract modified)

003929 Eroglu, L. Dept. of Pharmacology and Clinical Pharmacology, Istanbul Medical Faculty, University of Istanbul, Istanbul, Turkey **Effect of morphine on the brain histamine levels in stress-exposed rats.** Psychopharmacology. 63(1):13-15, 1979.

The effect of morphine on brain histamine levels in stress exposed rats (i.e. rats deprived of food from noon on the day preceding the experiment) was investigated. It seemed that the brain histamine level was not directly affected by stressors. However, morphine induced a sharp rise in the brain histamine levels in both morphine treated control and morphine treated stress groups. This effect of morphine was reversed by naloxone. This finding has a potential implication for the specificity of the interaction. 11 references. (Author abstract modified)

003930 Euvrard, C.; Premont, J.; Oberlander, C.; Boissier, J. R.; Bockaert, J. Centre de Recherche Roussel-UCLAF, F-93230 Romainville, France **Is dopamine-sensitive adenylate cyclase involved in regulating the activity of striatal cholinergic neurons?** Naunyn-Schmiedeberg's Archives of Pharmacology. 309(1):241-245, 1979.

Dopamine (DA) receptor mediated changes in striatal acetylcholine (ACh) levels were studied in male Sprague-Dawley rats to determine if this effect involves an adenylate cyclase dependent (D1) or independent (D2) type of DA receptor. Apomorphine and N-diphenethylamine derivatives increased striatal ACh levels in intact and 6-hydroxydopamine lesioned rats, but only apomorphine stimulated the adenylate cyclase activity of striatal homogenates. The N-diphenethylamine compounds had no effect on basal or DA stimulated activities of this enzyme. D-lysergic acid, which acts as a partial agonist of striatal DA sensitive adenylate cyclase, did not modify striatal ACh content. Intrastriatal injection of cholera toxin stimulated striatal adenylate cyclase without altering ACh concentrations. Haloperidol

and methergoline antagonized the DA stimulation of adenylate cyclase, but only haloperidol decreased striatal ACh levels. Results indicate that the DA receptor involved in regulating the activity of striatal cholinergic neurons is of the D2 type. 35 references. (Author abstract modified)

003931 Faingold, Carl L.; Stittsworth, James D., Jr. Dept. of Pharmacology, Southern Illinois University School of Medicine, P. O. Box 3926, Springfield, IL 62708 **Comparative effects of pentylenetetrazol on the sensory responsiveness of lateral geniculate and reticular formation neurons.** Electroencephalography and Clinical Neurophysiology. 49(1-2):168-172, 1980.

The responses of cat bulbar and mesencephalic reticular formation (MRF) neurons to visual, auditory, and/or somatosensory stimuli were considerably enhanced after subconvulsant doses of pentylenetetrazol (PTZ) in a similar fashion suggesting a general action of PTZ on reticular formation (RF) neurons. PTZ enhanced MRF responses evoked by electrical stimuli in the lateral geniculate nucleus (LGN) or cochlear nucleus but only modestly enhanced LGN neuronal responses. These findings indicate that the effects of this convulsant on the first brain sensory relay nuclei and primary sensory receptors do not appear to be sufficient to account for the extensive PTZ-induced enhancement of RF neuronal responses, and direct effects of PTZ on the reticular formation may play a major role in this enhancement. 11 references. (Author abstract modified)

003932 Fallert, M.; Bohmert, G.; Dinse, H. R. O.; Sommer, T. J; Bittner, A. Dept. of Physiology, University of Mainz, D-6500 Mainz, Germany **Microelectrophoretic application of putative neurotransmitters onto various types of bulbar respiratory neurons.** Archives Italiennes de Biologie. 117(1):1-12, 1979.

Six putative neurotransmitters (glycine, GABA, glutamate, dopamine, norepinephrine (NE), and serotonin (5-HT)), and the beta-receptor excitant isoproterenol were applied to rabbit bulbar respiratory neurons classified according to their burst discharge in the respiratory cycle and, for comparison, also to nonspecific cells. With glycine, inhibition occurred in inspiration (I) and prevailed in unspecific neurons. Following GABA, inhibition preponderated in I and expiration linked (E) neurons. Glutamate excited E neurons. With dopamine, inhibition prevailed in I and nonspecific neurons, while the majority of E neurons remained unaffected. With NE, excitation occurred in EI and proponderated in I, IE, E and nonspecific neurons, while some IE and E neurons were inhibited. The effects of isoproterenol did not allow any clear statement about receptor properties. In I units, however, activation was more frequent than inhibition. With 5-HT, excitation prevailed in IE neurons. About half of the I cells remained unaffected and in the remainder inhibition preponderated over activation. This suggests the existence of two 5-HT specific receptors in I and IE neurons. Comparison of the single effects revealed differences in the receptor properties of the various cell types. Results suggest that some cell types possess dopaminergic receptors and that these differ from NE receptors, which have been found in all cell types. NE receptor stimulation apparently can result in neuronal activation or inhibition. 32 references. (Author abstract modified)

003933 Farjo, I. B.; McQueen, Judith K. Dept. of Pharmacology & Therapeutics, University of Baghdad, Baghdad, Iraq **Dopamine agonists and cobalt-induced epilepsy in the rat.** British Journal of Pharmacology. 67(3):353-360, 1979.

Electrocorticogram recordings were made in conscious male Wistar rats made epileptic by cortical implants of cobalt prior to treatment with dopaminergic agonists. Apomorphine (0.5, 1.0, and 2.0mg/kg i.p.) and lisuride (0.1, 0.25, 0.5, and 1.0mg/kg i.p.) inhibited spike activity in established primary and secondary foci in a dose dependent manner. Bromocriptine (10 and 20mg/kg i.p.) and CF25-397 (40mg/kg i.p.) had a similar effect, but only after a latent period of several hours. Chronic administration of bromocriptine (20mg/kg/day i. p.) attenuated the normal development of foci following implantation. Pimozide (1mg/kg i.p.) potentiated the cortical epileptic activity in cobalt implanted rats and blocked the antiepileptic effects induced by the dopamine agonists.. Intrastriatal administration of dopamine (25mcg) or apomorphine (60mcg) suppressed epileptiform spikes in the cortex. Destruction of striatial catecholamine terminals by 6-hydroxydopamine increased the spike activity. It is concluded that the striatum may play an essential part in mediating the antiepileptic effects of dopamine and its agonists in this model of epilepsy. 34 references. (Author abstract modified)

003934 Fekete, Marton I. K.; Szentendrei, Tibor; Herman, Jean Paul; Kanyicska, Bela. H-1450 Budapest, P.O.B. 67, Hungary **Effects of reserpine and antidepressants on dopamine and DOPAC (3,4-dihydroxyphenylacetic acid) concentrations in the striatum, olfactory tubercle and median eminence of rats.** European Journal of Pharmacology. 64(4):231-238, 1980.

Levels of dopamine (DA) and 3,4-dihydroxyphenylacetic acid (DOPAC) were measured in the median eminence, olfactory tubercle, and rostral and caudal portions of the striatum of female CFY rats treated with reserpine, amitriptyline, nomifensine, and 1-benzyl-4-(2'-piridylcarbonyl)-piperazine (EGYT-475). Reserpine (1mg/kg i.p.) decreased DA in the median eminence, olfactory tubercle, and rostral striatum, but not in the caudal striatum. Amitriptyline and EGYT-475 antagonized the reserpine-induced depletion of DA in the olfactory tubercle. In the median eminence, amitriptyline attenuated the effect of reserpine, but nomifensine augmented it; EGYT-475 had no effect. The antidepressants antagonized the reserpine-induced increase of DOPAC in the rostral part of the striatum. 35 references. (Author abstract modified)

003935 Ferri, Sergio; Spampinato, Santi; Costa, Giovanni. Dept. of Pharmacology and Pharmacognosy, A. Doria Ed. 12, University of Catania, Catania, Italy **Changes induced by D-met2-pro5-enkephalinamide in plasma insulin response to glucose in the rat.** Biochemical Pharmacology. 28(22):3346-3347, 1979.

An analogue of met-enkephalin, D-Met2-pro5-enkephalinamide (Met-Enk-NH2), exerted an extrapituitary hormonal effect following i.v. administration to male Sprague-Dawley rats. Plasma insulin levels in rats treated with Met-Enk-NH2 were significantly lower than in control animals 3 minutes after glucose loading, the time of peak plasma insulin response. In samples taken 8 minutes after glucose injection, mean values of plasma insulin were significantly higher in the opioid treated rats than in controls. Plasma insulin values were similar in the two groups for the remainder of the observation period. Within 30 minutes of glucose injection, blood glucose concentration was elevated in the Met-Enk-NH2 treated rats, suggesting the analogue duplicates the hyperglycemic effect of morphine. 12 references.

003936 Fex, Jorgen; Martin, Michael R. Laboratory of Neuro-otolaryngology, NINCDS, NIH, Bethesda, MD 20205 **Lack of effect of DL-alpha-aminoadipate, an excitatory amino acid antagonist, on cat auditory nerve response to sound.** Neuropharmacology. 19(8):809-811, 1980.

DL-alpha-aminoadipate, locally applied to the cat cochlea at concentrations of 1mM and 10mM, had no effect on the amplitude, latency, or shape of click evoked auditory nerve compound action potentials at 5, 10, and 40dB above threshold. This suggests that the postsynaptic receptor of the hair cell/auditory nerve synapse is not of the N-methyl-D-aspartate (NMDA) pre-

ferring type. Responses to exogenously applied glutamate and aspartate reported in other studies may be due to an interaction with non-NMDA receptor at the hair cell/auditory nerve synapse or with an extrasynaptic receptor. 9 references. (Author abstract modified)

003937 Fields, Jeremy Z.; Reisine, Terry D.; Pedigo, Norman W.; Yamamura, Henry I. Department of Pharmacology, College of Medicine, University of Arizona Health Sciences Center, Tucson, AZ 85724 **Characterization of (3H)spiroperidol binding in the rat substantia nigra.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1605-1607).

The specific binding of (3H)spiroperidol was examined in male Sprague-Dawley rat substantia nigra (SN) and corpus striatum (CS). The binding sites in the two brain regions appeared to be kinetically similar, but the receptor density in the SN was only 10 to 15% of that in the CS. Drug inhibition studies indicated that (3H)spiroperidol labeled dopamine receptors in both regions. Lesion of the CS with intrastriatal kainic acid produced a dramatic loss of (3H)spiroperidol binding in the CS but did not alter binding in the SN. Results suggest that the (3H)spiroperidol binding in the SN is not located on striatonigral neurons and is not associated with dopamine sensitive adenylate cyclase. Preliminary studies suggest a large portion of the binding may be associated with dopamine cell bodies or dendrites. 6 references. (Author abstract modified)

003938 Fletcher, Allan; Fowler, Leslie J. Dept. of Pharmacology, School of Pharmacy, University of London, London, WC1N 1AX, England **Gamma-aminobutyric acid metabolism in rat brain following chronic oral administration of ethanolamine O-sulfate.** Biochemical Pharmacology. 29(11):1451-1454, 1980.

Chronic oral administration of ethanolamine O-sulphate (EOS) was found to result in a marked inhibition of rat whole-brain GABA transferase (GABA-T) activity and a significant increase in brain GABA concentrations. The maximum degree of GABA-T inhibition attained was 83%, when GABA levels were 200% of control values. A fixed dose of EOS produced a steady fall in GABA-T activity over the first 7 days of administration, when enzyme activity appeared to stabilize at 20% to 25% of control values. Concurrently, GABA levels rose to a steady maximum value of approximately 240% of control values. These changes were accompanied by significant increases in brain content of alanine and taurine. No behavioral changes were seen following chronic EOS administration. 19 references. (Author abstract)

003939 Fludder, Joan M.; Leonard, B. E. Leonard: Pharmacology Dept., University College, Galway, Republic of Ireland **Chronic effects of mianserin on noradrenaline metabolism in the rat brain: evidence for a pre-synaptic alpha-adrenolytic action in vivo.** Psychopharmacology. 64(3):329-332, 1979.

Chronic effects of mianserin on noradrenaline metabolism in rat brain were investigated, and the site of mianserin action was sought via study of the interaction of mianserin and the presynaptic alpha-adrenoreceptor agonist, clonidine. Chronic administration of clonidine decreases the concentration of the extraneuronal metabolite of noradrenaline normetanephrine in the amygdaloid cortex and increases it in the midbrain. Conversely, blockade of these presynaptic receptors by yohimbine increases the normetanephrine concentration in the amygdaloid cortex and decreases it in the midbrain. Mianserin had a qualitatively similar action to that of yohimbine. When given clinically to rats in combination with clonidine, mianserin antagonized both the depression of behavior of the rats in the open-field apparatus and also the effects of the alpha-agonist in reducing the concentration of normetanephrine in the amygdaloid cortex. It appears that the chronic effect of mianserin are due to an increase in noradrenaline release as a consequence of the inhibition of presynaptic alpha-adrenoreceptors. 19 references. (Author abstract modified)

003940 Fowler, Christopher J.; Oreland, Lars. Dept. of Pharmacology, University of Umea, S-901 87 Umea, Sweden **The nature of the substrate-selective interaction between rat liver mitochondrial monoamine oxidase and oxygen.** Biochemical Pharmacology. 29(16):2225-2233, 1980.

The nature of substrate selective interaction between rat liver mitochondrial monoamine oxidase (MAO) and oxygen was investigated. The activity of rat liver MAO was increased in an uncompetitive manner with increasing concentrations of oxygen. However, the value of the Michaelis constant for oxygen, estimated from determinations of enzyme activity with six oxygen concentrations and five to six amine substrate concentrations, was dependent upon the amine substrate used to assay for activity. In an attempt to determine the nature of these differences, the value of the Michaelis constants for oxygen have been related to the rate constant of the limiting step in the overall enzyme catalysed reaction values of the enzyme towards the different amine substrates. Results are consistent with the hypothesis that the two forms of MAO in rat liver are not independent enzyme forms, but interact one with the other in some way. 50 references. (Author abstract modified)

003941 Frances, H.; Puech, A. J.; Chermat, R.; Simon, P. Dept. de Pharmacologie, Fac. de Medecine Pitie-Salpetriere, 91 Bd. de l'Hopital, F-75634 Paris Cedex 13, France **/Effects of four beta-blocking agents on some psychopharmacological tests in mice./** Effets de quatre bloqueurs beta-adrenergiques sur quelques tests de psychopharmacologie chez la souris. Psychopharmacology. 63(1):43-48, 1979.

Common effects of four beta adrenergic blocking drugs were investigated in mice using classical and new psychopharmacological tests. Propranolol, alprenolol, practolol and penbutolol reduced the increase in locomotor activity produced by reserpine after monoamine oxidase inhibition, produced hypothermia when associated with amphetamine, and increased oxotremorine-induced hypothermia. The order of potency indicated that penbutolol was greater than propranolol which was greater than alprenolol which was greater than practolol. Propranolol and penbutolol decreased the toxicity provoked in crowded mice by amphetamine or by the association pargyline/reserpine; alprenolol and practolol did not. Propranolol, penbutolol and alprenolol antagonized the amphetamine-induced increase in motor activity; practolol did not. It is suggested that for the selection of a beta blocking drug, regarding central effects in man, the tests described deserve consideration. 34 references. (Journal abstract modified)

003942 Frankhuyzen, Abraham L.; Mulder, Arie H. Dept. of Pharmacology, Free University, Medical Faculty, Van der Boechorststraat 7, 1081 BT, Amsterdam, The Netherlands **Noradrenaline inhibits depolarization-induced 3H-serotonin release from slices of rat hippocampus.** European Journal of Pharmacology. 63(2/3):179-182, 1980.

The deplorization-induced release of tritiated serotonin (5-HT) and noradrenaline (NA) from slices of male Wistar rat hippocampus was studied. In the presence of desipramine, exogenous NA inhibited the release of both labeled amines by more than 70%. Both these effects were competitively antagonized by phentolamine, but not by propranolol. It is suggested that the inhibitory effect of NA on 3H-5HT release from hippocampal slices reflects the activation of postsynaptic alpha-recep-

tors localized on serotonergic nerve terminals. 11 references. (Author abstract modified)

003943 Freer, Lawrence Sturdevant. Georgetown University Medical Center **Characterization of the functional tolerance development to N,N'-dimethoxymethyl phenobarbital. (Ph.D. dissertation).** Dissertation Abstracts International. 40(5):2146-B, 1979. Ann Arbor, Univ. Microfilms No. 7923000, 288p., 1979.

The relative degree of CNS depressant activity demonstrated by Eterobarb (N,N'-dimethoyxmethylphenobarbital) (DMMP) and its two major metabolites, phenobarbital (PB) and N-monomethoxymethyl-phenobarbital (MMP) were studied in the rat. The possible contribution of the interactions between the primary drug and its metabolites and/or the role of functional tolerance development to the diminished CNS depressant activity observed with DMMP were also examined. Results indicate that DMMP demonstrates a markedly reduced degree of CNS depressant activity compared to PB. Under certain circumstances DMMP was found to diminish the CNS activity of PB; the type of interaction is quite complex and seems to be affected by changes in dose levels of administered MMP, but not by differences in the latency to loss of the righting reflex. Both the rate and magnitude of functional tolerance development following DMMP were apparently increased over that observed for administered PB when administered chronically, resulting in a greater decrease in CNS depressant activity. (Journal abstract modified)

003944 Freund, J. L.; Freund, D.; Hofmann, R.; Kahlau, F.; Glanzmann, P. Institut f. Arbeitsphysiologie u. Rehabilitationsforschung. Universitat Marburg, Ketzerbach 21, D-3550 Marburg/Lahn, Germany /Influence of behavior changing drugs, imipramine and tranylcypromine, on the composition of the blood and the activity of the alkaline leucocytophosphatase in adult male Wistar rats./ **Einfluss verhaltensandernder Psychopharmaka -- Imipramin und Tranylcypromin -- auf das Blutbild und auf die Aktivitat der alkalischen Leukozytne/phosphatase bei emotiven und nichtemotiven Wistar-Ratten.** Arzneimittel Forschung. 29(11):1727-1732, 1979.

The corpuscular composition of the blood and the alkaline leucocytophosphtase (ALP) activity was measured for 40 emotive and nonemotive adult male Wistar rats to test the influence of imipramine (IMI) and tranylcypromine (TRAN) in a single dose and given for a period of 8 days. Special attention was paid to the kind of reaction of the animals. Changes in the red and white components of the blood were found due to drug application and to reaction type. The relationship between reaction type and drug application which was assumed to exist is confirmed. The ALP activity also changed depending on the type of drug dosage. The assumption that ALP activity is higher for emotive rats than for nonemotive ones is also confirmed. 20 references. (Author abstract modified)

003945 Fuller, Ray W.; Hemrick-Luecke, Susan. Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46285 **Long-lasting depletion of striatal dopamine by a single injection of amphetamine in iprindole-treated rats.** Science. 209(4453):305-307, 1980.

A single injection of amphetamine given to rats treated concurrently with iprindole so that they could not metabolize the amphetamine by para-hydroxylation resulted in a decrease in the concentration of striatal dopamine 1 week later. The decrease was antagonized by amfonelic acid, an inhibitor of uptake into dopamine neurons. The long lasting depletion of cerebral dopamine by amphetamine may be analogous to the depletion of cerebral serotonin by halogenated derivatives of amphetamine. The recognition that a single dose of amphetamine can cause long lasting, possibly neurtoxic changes in certain brain neurons may be of value in exploring a neurochemical basis for persistent behavioral changes in chronic amphetamine abusers. 12 references. (Author abstract modified)

003946 Garcia-Bunuel, Luis. Neurology Service, V.A. Medical Center, Portland, OR 97201 **Dopamine auto- and postsynaptic receptors: possible interference by gallamine.** Science. 209(4457):720, 1980.

Questions raised by the use of gallamine in a study on dopaminergic autoreceptors are discussed. It has been suggested that dopaminergic autoreceptors in the substantia nigra are much more sensitive to small doses of dopamine agonists than many of the postsynaptic dopaminergic receptors in the caudate nucleus. However, gallamine, which is widely used because of its blocking action of acetylcholine at the muscle end plate receptors also has a anticholinergic action as well. Because of this, its use in a study of central dopaminergic mechanisms raises doubts about the validity of these results. 7 references.

003947 Gent, J. P.; Phillips, N. I. Dept. of Pharmacology, Worsley Medical and Dental Building, University, Leeds LS2 9JT, England **Sodium di-n-propylacetate (valproate) potentiates responses to GABA and muscimol on single central neurones.** Brain Research. 197(1):275-278, 1980.

The actions of di-n-propylacetate (DPA, valproate), a well established, clinically useful anticonvulsant, on the activity of single neurons in the medullary reticular formation of rats were assessed. Neurons were chosen for study if they showed spontaneous activity and were sensitive to microiontophoretically applied GABA. During the microiontophoretic application of DPA, the depressant effects of GABA were repeatedly potentiated on 44 out of 48 neurons. Inhibitory responses to muscimol were also potentiated by DPA on 24 out of 26 cells. GABA responses were increased in amplitude, on different neurons, by 11% to 170% and muscimol responses by 12% to 180%. On cells on which GABA or muscimol responses were potentiated by DPA, DPA had no effect on control inhibitory responses to glycine. It is suggested that the potentiation of GABA responses may be mediated by an action of DPA at the GABA receptor complex, possibly at a modulator site, as has been proposed for the benzodiazepines. It is noted that the potentiation of GABA mediated neurotransmission may contribute to the anticonvulsant actions of DPA. 13 references.

003948 German, D. C.; Harden, H.; Sanghera, M. K.; Mann, D.; Kiser, R. S.; Miller, H. H.; Shore, P. A. Dept. of Physiology, University of Texas Health Science Center, 5323 Harry Hines Boulevard, Dallas, TX 75235 **Dopaminergic neuronal responses to a non-amphetamine CNS stimulant.** Journal of Neural Transmission. 44:39-49, 1979.

The effects of d-amphetamine (d-AMP) and the potent non-amphetamine CNS stimulant, amfonelic acid (AFA), on neostriatal DA metabolism (dihydroxyphenylacetic acid -- DOPAC) were compared. Results indicate that AFA, like d-AMP, reduces the firing rate of DA neurons, although unlike d-AMP, AFA does not cause a decrease in neostriatal DOPAC content and, in fact, enhances that produced by haloperidol (HALO). The AFA-induced decrease in firing rate, like d-AMP, is reversed by the DA receptor blocker HALO, but again unlike d-AMP, the decrease in firing rate is not prevented by catecholamine synthesis inhibition with alpha-methyl-para-tyrosine. Thus, both amphetamine and AFA have identical electrophysiological effects on DA neurons but act by different mechanisms. 27 references. (Author abstract modified)

003949 Gibb, J. W.; Kogan, F. J. Dept. of Biochemical Pharmacology and Toxicology, University of Utah, Salt Lake City,

UT 84112 **Influence of dopamine synthesis on methamphetamine-induced changes in striatal and adrenal tyrosine hydroxylase activity.** Naunyn-Schmiedeberg's Archives of Pharmacology. 310(2):185-187, 1979.

Large doses of methamphetamine decreased striatal tyrosine hydroxylase (TH) activity in male Sprague-Dawley rats. This effect was blocked by pretreatment with alpha-methyl-p-tyrosine. However, the increase in TH activity induced by methamphetamine in the adrenal gland was not prevented by inhibition of catecholamine synthesis. It is suggested that endogenous dopamine inhibits TH activity by activating presynaptic or postsynaptic dopamine receptors in the neostriatum, resulting in activation of the neuronal feedback pathway. Alternatively, dopamine may act on dendrodendritic autoreceptors in the substantia nigra. 15 references. (Author abstract modified)

003950 Greer, Charles A.; Alpern, Herbert P. Alpern: Institute for Behavioral Genetics, University of Colorado, Boulder, CO 80309 **Maturational changes related to dopamine in the effects of d-amphetamine, cocaine, nicotine, and strychnine on seizure susceptibility.** Psychopharmacology. 64(3):255-260, 1979.

The effects of four neural excitants (d-amphetamine, cocaine, nicotine, and strychnine) on myoclonic and clonic seizure susceptibility were investigated in two age groups (30 and 120 days) of short sleep mice. Amphetamine and cocaine decreased susceptibility to myoclonus in young mice and increased susceptibility in mature mice. These effects were attenuated by pretreatment with haloperiodol, indicating mediation by a dopaminergic system. Amphetamine did not alter clonic susceptibility in either age group of mice, whereas cocaine affected clonic susceptibility and myoclonus. The effects were not attenuated by haloperiodol, indicating mediation by systems other than dopamine. Nicotine decreased susceptibility to myoclonus and increased susceptibility to clonus, whereas strychnine increased susceptibility to both types of seizure. Haloperidol, however, failed to alter any of these effects. These results are consistent with previous work suggesting that a dopaminergic mechanism in these mice undergoes marked developmental change between 30 and 120 days of age. 43 references. (Author abstract modified(

003951 Guynn, Robert W.; Faillace, Louis A. Dept. of Psychiatry, University of Texas Medical School, Health Science Center, Houston, TX 77025 **The effect of the combination of lithium and haloperidol on brain intermediary metabolism in vivo.** Psychopharmacology. 61(2):155-159, 1979.

The effect of the chronic administration of the comination of lithium and haloperidol was studied in rat brain in vivo. Lithium was administered in food in amounts sufficient to maintain serum lithium levels of 1.0 plus or minus 0.1mEq/1; haloperidol (l.5mg/kg) was given i.p. once daily. Control animals pair fed with the lithium/haloperidol group received either lithium alone, haloperidol alone, or neither drug. Fifteen days after the beginning of the experiments, the brains were instantaneously frozen with a rapid brain freezing device and multiple metabolites were measured in the perchloric acid extract of the tissue. Intermediates examined included selected metabolites of the glycolytic pathway and the tricarboxylic acid cycle, N-acetylaspartate and cofactors such as ATP, CoA, and acetyl-CoA. Estimates of the effects of the treatments of cytoplasmic and mitochondrial redox states were also made. Results show only minor effects of any of the treatments on any of the parameters studied and little or nothing to distinguish the combination of lithium and haloperidol from either treatment alone. 40 References. (Author abstract)

003952 Hall, Edward D. Program in Pharmacology, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 **Glucocorticoid modification of the responsiveness of a fast (type 2) neuromuscular system to edrophonium and d-tubocurarine.** Experimental Neurology. 69(2):349-358, 1980.

The effects of intensive triamcinolone diacetate pretreatment regimen in cats were examined on the facilitatory actions of edrophonium and the blocking effects of d-tubocurarine in a fast (type 2) neuromuscular system, the in vivo gastrocnemius/plantaris nerve/muscle preparation. In glucocorticoid treated animals, i.v. edrophonium responsiveness, which was measured in terms of the potentiation of the indirectly evoked maximal muscle contractile tension, was significantly decreased compared with that in untreated cats. In contrast, the neuromuscular blocking potency of i.v. d-tubocurarine was reduced after triamcinolone treatment. Twice as much drug was required to achieve the same degree of reduction indirectly evoked muscle tension. The decreased facilitatory potency of edrophonium was indicative of a glucocorticoid decrease in the excitability of type 2 motor neuron terminals. The decreased potency of d-tubocurarine, however, suggested an improvement in the evoked release of transmitter by single impulses and was in agreement with earlier work in soleus preparations. Taken together, the present data demonstrate the complexities of the direct effects of glucocorticoids on neuromuscular function. 21 references. (Author abstract modified)

003953 Hamilton, Murray G.; Hirst, Maurice; Blum, Kenneth. Southwest Foundation for Research and Education, West Loop 410 at Military Dr., San Antonio, TX 78284 **Opiate-like activity of salsolinol on the electrically stimulated guinea pig ileum.** Life Sciences. 25(26):2205-2210, 1979.

The activity of the tetrahydroisoquinoline compound, salsolinol, was investigated on the electrically stimulated guinea-pig ileum, an in vitro preparation known to be sensitive to opiate compounds. Previous research has suggested that salsolinol and narcotic agonists have a biochemical mechanism of action in common. Contractions elicited by electrical stimulation of the ileum were reduced partially by salsolinol. This action was antagonized by pretreatment with the narcotic antagonist, naloxone, but not reversed by this agent once the effect was initiated. In addition, salsolinol reduced the inhibitory activity of morphine. These results suggest that salsolinol may be a partial agonist on this opiate sensitive preparation. This effect assumes particular importance with the recent demonstration that a metabolite of salsolinol is present in the central nervous system of mice exposed chronically to alcohol. 27 references. (Author abstract modified)

003954 Harada, Masatomi; Maeno, Hiroo. Dept. of Pharmacology and Biochemistry, Yamanouchi Pharmaceutical Co., Ltd., Itabashi-ku, Tokyo 174, Japan **Biochemical characteristics of a potential antidepressant, 2-(7-indenyloxymethyl)morpholine hydrochloride (YM-08054-1).** Biochemical Pharmacology. 28(17):2645-2651, 1979.

The biochemical effects of a potential antidepressant, 2-(7-indenyloxymethyl)morpholine hydrochloride (YM-08054-1) were compared with those of viloxazine, a structural analogue, and of several tricyclic antidepressants. At concentrations less than 1mcM, YM-08054-1 and amitriptyline inhibited 5-hydroxytryptamine (5-HT) uptake by synaptosomes from hippocampus; viloxazine and iprindole were weak inhibitors of 5-HT and NA uptake. Amitriptyline and YM-08054-1 were much less potent than methamphetamine and tyramine in releasing labeled 5-HT from preloaded hypothalamic slices or labeled NA from preloaded hippocampal slices. Tricyclic antidepressants preferentially inhibited type-B monoamine oxidase (MAO) activity, but

YM-08054-1 was a weak inhibitor of both type-A and type-B MAO. 30 references. (Author abstract modified)

003955 Harston, Craig T.; Morrow, Anne; Kostrzewa, Richard M. East Tennessee State University, College of Medicine, Dept. of Pharmacology, Johnson City, TN 37601 **Enhancement of sprouting and putative regeneration of central noradrenergic fibers by morphine.** Brain Research Bulletin. 5(4):421-424, 1980.

Norepinephrine levels were elevated in the cerebellum and hindbrain of adult Simonsen rats treated at birth with 6-hydroxydopa (6-OHDOPA, 60mcg/g i.p.). Concurrent morphine sulfate treatment (20mcg/g i.p.) potentiated the response to 6-OHDOPA in the cerebellum and pons/medulla. Neonatal morphine treatment also increased the sprouting of noradrenergic neurons in the 6-OHDOPA treated rats. 27 references. (Author abstract modified)

003956 Hart, S. L.; Kitchen, I.; Waddell, P. R. Basic Medical Sciences Group, Dept. of Pharmacology, Chelsea College, University of London, London, SW3 6LX, England **Different effects of current strength on inhibitory responses of the mouse vas deferens to methionine- and leucine-enkephalin.** British Journal of Pharmacology. 66(3):361-363, 1979.

The inhibitory potency of methionine-enkephalin on the field stimulated mouse vas deferens was greatly increased by a reduction in current strength. In contrast, the inhibitory potency of leucine-enkephalin was only slightly increased when current strength was reduced. These results suggest that methionine-enkephalin and leucine-enkephalin are not commonly mediated in the mouse vas deferens. This differential response to reductions in current strength may provide a rapid method for ascertaining the heterogeneity of enkephalin extracts. 10 references. (Author abstract modified)

003957 Hayashi, Toshiharu; Negishi, Koroku. Negishi: Neuroinformation Research Institute, University of Kanazawa School of Medicine 13-I Takara-machi, Kanazawa 920, Japan **Suppression of retinal spike discharge by dipropylacetate (Depakene): a possible involvement of GABA.** Brain Research. 175(2):271-278, 1979.

Effects of dipropylacetate (DPA) were studied on spike discharges in the isolated carp retina. When applied electrophoretically or by pressure microinjection in the vicinity of the recording electrode at the inner plexiform layer, DPA consistently activated spike discharges. When introduced into the perfusate, DPA produced complex actions: some units responded to DPA with an initial activation followed by suppression of spike discharges. When GABA was applied electrophoretically together with perfusion of DPA, the depressant effect was greater than that obtained with each of these compounds alone. Bicuculline in the perfusate markedly attenuated the depressant actions of GABA and DPA, alone or in combination. It is concluded that the delayed suppression of spike discharges by perfused DPA is mediated by GABA receptors on ganglion cells in the carp retina. 19 references. (Author abstract modified)

003958 Heavner, James E.; Bloedow, Duane C. Anesthesiology and Anesthesia Research, University of Washington, Seattle, WA 98195 **Ketamine kinetics: decerebrate vs. intact cats.** Canadian Journal of Physiology and Pharmacology. 57(8):878-881, 1979.

The pharmacokinetics of ketamine (10mg/kg i.v.) were compared in decerebrate and intact cats. A two compartment model best described the data in both groups. The apparent volume of distribution of the drug in the body, and half-life of the postdistributive phase were significantly decreased in the decerebrate animals. These results emphasize the importance of correlating behavior and neuronal activity with plasma or blood concentrations of drug in animals prepared for study by methods likely to alter physiological parameters. 9 references. (Author abstract modified)

003959 Hellstrom, Sten; Hanbauer, Ingeborg. Department of Anatomy, University of Umea, S-901 87 Umea, Sweden **Role of dopamine and norepinephrine in carotid body.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1539-1541).

Mass fragmentography was used to study catecholamines in the rat carotid body. Ganglionectomy reduced the norepinephrine (NE) content in the carotid body by about 50%, but did not alter the dopamine (DA) content. Hypoxia decreased the DA content of the carotid body without affecting the rate of DA turnover and had no effect on NE level or turnover. The decrease in DA concentration appeared to be independent of innervation of the carotid body by the carotid sinus nerve or superior cervical ganglion. Results suggest that hypoxia causes DA release from glomus cells. 2 references. (Author abstract modified)

003960 Hemmingsen, Ralf; Barry, David I.; Hertz, Marianne M. Dept. of Psychiatry, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen O, Denmark **Cerebrovascular effects of central depressants: a study of nitrous oxide, halothane, pentobarbital and ethanol during normocapnia and hypercapnia in the rat.** Acta Pharmacologica et Toxicologica. 45(4):287-295, 1979.

The effects of the central depressant nitrous oxide, halothane, pentobarbital, and ethanol on cerebral blood flow, cerebral oxygen consumption (CMR02), and cerebral vascular reactivity to carbon dioxide were measured in male Wistar rats, using the rapid and repetitive intraarterial 133Xenon injection technique. Cerebrovascular resistance during normocapnia in the pentobarbital group was significantly higher than in the nitrous oxide group, indicating a vasoconstrictor effect for pentobarbital that may explain the protective properties of barbiturates against cerebral ischemia. Results indicate that pentobarbital and ethanol may act synergistically with carbon dioxide in depressing CMR02 and vascular reactivity. 29 references. (Author abstract modified)

003961 Hendrickson, Constance M.; Lin, Shin. Dept. of Biophysics, Johns Hopkins University, Baltimore, MD 21218 **Opiate receptors in highly purified neuronal cell populations isolated in bulk from embryonic chick brain.** Neuropharmacology. 19(8):731-739, 1980.

The binding of (3H)naloxone to neuronal and nonneuronal cell populations isolated in bulk from embryonic chick brain was examined. Results indicated that the isolated neuronal cells had opiate receptors similar to those found in rat brain. No specific opiate binding activity was found in the isolated nonneuronal cells. 20 references. (Author abstract modified)

003962 Henry, James L.; Sessle, Barry J.; Lucier, Gregory E.; Hu, James W. Dept. of Research in Anaesthesia, McGill University, 3655 Drummond Street, Montreal, Quebec H3G 1Y6, Canada **Effects of substance P on nociceptive and non-nociceptive trigeminal brain stem neurons.** Pain. 8(1):33-45, 1980.

The effects of glutamate and substance P on single neurons in the trigeminal nuclei oralis and caudalis were studied in cats anesthetized with chloralose and paralyzed. Neuronal responses to natural noxious and innocuous cutaneous and intraoral stimulation, as well as to bipolar stimulation of the ipsilateral and contralateral canine tooth pulps, the exposed infraorbiatl and superior laryngeal nerves, and forepaw. Glutamate excited all units tested. Substsnce P also had excitatory effects, but only on

some units. The slow time course of this effect was similar to that reported in other CNS regions. Units excited by substance P were located only in nucelus caudalis, and all responded to noxious cutaneous stimuli and/or stimulation of the tooth pulp; units responding only to innocouous orofacial stimulation were not excited by substance P. Levorphanol and opiod peptides, applied iontophoretically to some of the units, were found to have depressant effects on nociceptive units. Data support the possibility that substance P and the endogenous opioids play a role in chemical transmission in nociceptive pathways in trigeminal nucleus caudalis. Implications of the regional and functional specificity of substance P excitation are also discussed. 40 references. (Author abstract modified)

003963 Herberg, L. J.; Wishart, T. B. Experimental Psychology Laboratory, Institute of Neurology, Queen Square, London WC1N 3BG, England **Selective permeation of the blood-brain barrier as a cause of the anomalous properties of atypical neuroleptics.** Pharmacology Biochemistry and Behavior. 12(6):871-873, 1980.

The depressions of hypothalamic self-stimulation produced by metoclopramide and by a typical neuroleptic, spiroperidol, when injected by different routes were compared. Metoclopramide was found to be nearly 30 times more potent when administered directly into the brain via the cerebral ventricles than when injected intraperitoneally; on the other hand, the potency of spiroperidol was virtually unaffected by the route of administration. The blood-brain barrier is known to be absent from brain sites controlling emesis and prolactin secretion; thus the potency of metoclopramide as an antiemetic and in releasing prolactin, and its relative ineffectiveness as an antipsychotic can be accounted for by a failure to enter the brain freely except at privileged sites. Thus, its anomalous properties are not necessarily inconsistent with the dopamine theory of schizophrenia. 30 references. (Author abstract modified)

003964 Herman, Zbigniew S.; Slominska-Zurek, Jadwiga. Dept. of Pharmacology, Biological-Physiological Institute, Silesian Medical Academy in Katowice, Marksa 38, 41-808 Zabrze, Poland **Central cholinergic receptor supersensitivity after long-term atropine administration.** Psychopharmacology. 64(3):337-340, 1979.

Central cholinergic receptor supersensitivity following long-term atropine (AT) administration was investigated in rats. Rats were treated with a single dose of AT (5mg/kg), or a daily administration of this dose for 14 or 31 days. Three hours after the single dose and 24 hours after the last dose of chronically administered AT, 10mg of acetylcholine (ACh) was injected intracerebroventricularly and animal behavior was assessed. The tremorigenic effect of oxotremorine was also measured in mice treated with 10mg/kg of AT for 1 month. It was shown that a single dose of AT antagonized ACh-induced behavior. The long-term treatment with AT enhanced the depressive behavior of ACh in rats and the tremorigenic effect of oxotremorine in mice. Results suggest that long-term blockade of central cholinergic receptors induces their hypersensitivity. 12 references. (Author abstract modified)

003965 Hery, F.; Soubrie, P.; Bourgoin, S.; Motastruc, J. L.; Artaud, F.; Glowinski, J. INSERM U.6, 280, Bld Ste Marguerite, F-13009 Marseille, France **Dopamine released from dendrites in the substantia nigra controls the nigral and striatal release of serotonin.** Brain Research. 193(1):143-151, 1980.

Unilateral application of dopamine reduced the release of (3H)serotonin in the ipsilateral substantia nigra and caudate nuclei of encephale isole cats. Alpha-methylparatyrosine stimulated the release of (3H)serotonin in these structures. Both treatments decreased (3H)serotonin release in the contralateral caudate nucleus, but not in the contralateral substantia nigra. It is suggested that these effects are related to changes in the activity of nigroraphe neurons regulated by dopamine released from dendrites of the nigrostriatal dopaminergic neurons. 39 references. (Author abstract modified)

003966 Hommer, D. W.; Bunney, B. S. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Effect of sensory stimuli on the activity of dopaminergic neurons: involvement of non-dopaminergic nigral neurons and striato-nigral pathways.** Life Sciences. 27(5):377-386, 1980.

The effects of sciatic nerve stimulation on the activity of dopaminergic and nondopaminergic neurons in the rat substantia nigra were studied using single unit recording techniques. The stimulation-induced changes in zona compacta dopaminergic neuron activity usually consisted of an initial inhibitory period followed by one or more oscillations between excitation and inhibition. These oscillations were attenuated by parenterally administered haloperidol or by a lesion which destroyed striato-nigral pathways. The initial inhibitory period was decreased by haloperidol and increased by the lesion. Nondopaminergic zona reticulata neurons responded to stimulation with an initial excitation which had a latency similar to the latency of the initial inhibition of dopaminergic neurons. These results suggest that sensory stimuli may induce and initial inhibition of dopaminergic neurons, at least in part, through excitation of an inhibitory non-dopaminergic zona reticulata neuron. The subsequent oscillations appear to be mediated through reciprocal striato-nigral, nigro striatal pathways. 21 references. (Author abstract modified)

003967 Horodnicki, Jan M.; Wasik, August; Firko, Marek; Janicka, Barbara. Klinika Psychiatrii AM, ul. Broniewskiego 32, 71-460 Szczecin, Poland /The effect of lithium ions on the activity of glycolate enzymes in the brain and in peripheral blood leukocytes in rats./ **Wplyw jonow litu na aktywnosc enzymow glikolizy w mozgu i leukocytach krwi obwodowej szczurow.** Psychiatria Polska. 13(6):543-548, 1979.

Lithium carbonate was administered to Wistar rats for over 8 days, using a stomach probe at doses of 2mEg/kg, in order to study the effect the of lithium ions on the activity of glycolate enzymes in rat brain and in the peripheral blood leukocytes. The mean lithium concentrations in mEq/1 of blood serum, erythrocytes, and brain amounted in 7 animals to 1.43 plus or minus 0.8; 1.13 plus or minus 0.65; and 0.92 plus or minus 0.54, respectively. Comparison with control animals showed that lithium ions had brought about a statistically significant increase in the mean activities of HK and ALD in leucocyte homogenates and of G-6-PDH and GAPDH in brain homogenates. No statistically significant differences between the two groups of animals were found in the mean activities of PGM, TK, PHI, PFK, and PK. The mean value of the HK activity indicator, calculated from the quotient of enzyme activity in the brain and leukocytes in each animal, was half that found in control animals, while the value of the GAPDH indicator was three times larger than in control animals. 23 references. (Journal abstract modified)

003968 Hruska, Robert E.; Ludmer, Lynn M.; Silbergeld, Ellen K. Neurotoxicology Section, NINCDS, NIH, Building 36, Room 4A22, Bethesda, MD 20205 **Characterization of the striatal dopamine receptor supersensitivity produced by estrogen treatment of male rats.** Neuropharmacology. 19(9):923-926, 1980.

Estrogen treatment of male Sprague-Dawley rats increased the number of striatal dopamine (DA) receptors without altering their affinity. This effect only occurred in vivo, and only the beta-diastereomer of 17-estradiol was active. The presynaptic

uptake of DA was not altered, and other striatal receptors showed no changes. Hypophysectomy completely blocked the effect of estrogen on striatal DA receptors and on stereotypy. Results are discussed in relation to the chorea associated with pregnancy and with use of oral contraceptives. 10 references. (Author abstract modified)

003969 Huang, J. T. Center for Neurochemistry, Rockland Research Institute, Wards Island, NY 10035 **Accumulation of amino acids, met-enkephalinamide and morphine in choroid plexus: effect of pretreatment with phosphatidylcholine vesicles.** Research Communications in Chemical Pathology and Pharmacology. 28(3):567-570, 1980.

The effect of phosphatidylcholine vesicles (liposomes) on the accumulation of amino acids, met-enkephalinamide, and morphine in the Sprague-Dawley rat choroid plexus was examined. The accumulation of alpha-aminoisobutyric acid, tyrosine, and morphine decreased when the choroid plexus was preincubated with liposomes, but not with liposomes containing cholesterol. The accumulation of met-enkephalinamide was not affected in either case. 9 references. (Author abstract modified)

003970 Huff, Rita M.; Adams, Ralph N. Dept. of Pharmacology and Toxicology, University of Kansas, Lawrence, KS 66045 **Dopamine release in N. accumbens and striatum by clozapine: simultaneous monitoring by in vivo electrochemistry.** Neuropharmacology. 19(6):587-590, 1980.

The effects of clozapine and chlorpromazine on dopamine release in N. accumbens vs. caudate were examined by in vivo electrochemistry. Chloropromazine produced strong increases in electrochemical signal in both caudate and N. accumbens, whereas clozapine gave a dose related increase in N. accumbens, but little or not change in caudate. The clozapine-induced electrochemical signals in the N. accumbens were abolished by 6-hydroxydopamine lesioning of the A10 regions. Results support the contention that clozapine acts preferentially in the limbic dopaminergic system. 10 references. (Author abstract)

003971 Hyttel, John; Christensen, Anne Vibeke; Fjalland, Bjarne. Dept. of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500 Valby, Denmark **Neuropharmacological properties of amitriptyline, nortriptyline and their metabolites.** Acta Pharmacologica et Toxicologica. 47(1):53-57, 1980.

Amitriptyline, nortriptyline, and their metabolites were tested for inhibitory effects on the uptake of serotonin (5-HT) in rabbit thrombocytes and noradrenaline (NA) in mouse atria and heart, for anticholinergic activity in guinea-pig ileum, and for antagonism of tetrabenazine-induced inactivity and apomorphine and 5-hydroxytryptophan potentiating effects in mice. Amitriptyline inhibited 5-HT and NA uptake equally, but nortriptyline had more potent effects on NA than 5-HT uptake; 10-hydroxyamitriptyline and 10-hydroxynortriptyline resembled nortriptyline in this respect. The 10-hydroxylated metabolites amitriptyline-N-oxide, and desmethylnortriptyline had weaker anticholinergic effects than amitriptyline and nortriptyline. Results of the behavioral tests were generally consistent with these in vitro findings. 24 references. (Author abstract modified)

003972 Ikeda, S. R.; Aronstam, R. S.; Eldefrawi, M. E. Eldefrawi: Dept. of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD 21201 **Nature of regional and chemically-induced differences in the binding properties of muscarinic acetylcholine receptors from rat brain.** Neuropharmacology. 19(6):575-585, 1980.

The binding and biochemical properties of muscarinic acetylcholine receptors in membranes from rat brain cerebral cortex and brainstem, as well as in cortex membranes treated with 1mM N-ethyl maleimide (NEM), were investigated using dl(3H)-3-quinuclidinyl benzilate ((3H)-QNB). Although cortex and brainstem receptors displayed multiple affinities for most agonists, the fraction of receptors in each affinity state varied with the agonist, and the apparent affinity constant for each state was often not the same in receptors from the two brain areas. Reductive alkylation of cortex membranes with NEM always increased agonist affinity and increased the fraction of receptors in the high affinity state. However, NEM treatment also altered agonist binding constants in a nonsystematic manner. With both enantiomers of one agonist (C13CD), the usual order of receptor agonist affinity (brainstem greater than cortex) was reversed, and treatment of cortex with NEM further increased this difference in affinity. Brainstem and cortical receptors differed greatly in their sensitivity to the monovalent and divalent cation content of the binding medium, and these differences were not affected by NEM treatment. It is concluded that a simple, two state model of muscarinic receptors involving high and low agonist affinity populations does not afford a complete description of the regional and chemically-induced differences in receptor binding properties. 23 references. (Author abstract)

003973 Illes, Peter; Zieglgansberger, Walter; Herz, Albert. Dept. of Neuropharmacology, Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 2, D-8000 Munich 40, Germany **Lack of cross-tolerance between morphine and Leu-enkephalin in the mouse vas deferens.** Brain Research. 197(1):260-263, 1980.

The effect of Leu-enkephalin on excitatory junction potentials (ejp) amplitudes of vasa deferentia prepared from morphine treated mice was investigated to assess cross-tolerance between morphine and Leu-enkephalin. Results indicate the lack of any significant cross-tolerance between morphine and Leu-enkephalin in the mouse vas deferens. Leu-enkephalin shifted the stimulus/response curves in a parallel way to the right both in preparations from naive and morphine treated mice with no difference in stimulus ratios. Results are consistent with the recent finding that the contractile response of the mouse vas deferens shows marked tolerance with long-term in vivo exposure to either sufentanyl (mu receptor agonist) or D-A1a2-D-Leu5-enkephalin (delta receptor agonist) without any significant cross-tolerance between the two agonists. 14 references.

003974 Illsley, Nicholas P.; Lamartiniere, Coral A. Laboratory of Environmental Toxicology, NIEHS, Research Triangle Park, NC 27709 **Prenatal programming of hepatic monoamine oxidase by 5,5-diphenylhydantoin.** Biochemical Pharmacology. 28(17):2585-2590, 1979.

The effects of 5,5-diphenylhydantoin (DPH) on hepatic monoamine oxidase (MAO) activity in developing Sprague-Dawley rats were determined. In untreated rats, liver MAO increased gradually in both sexes until puberty; after puberty, MAO activity was 1.5 to 2.0 times greater in females than in males. Oral administration of 10mg/kg DPH to pregnant rats on days 7, 9, 12, 14, and 16 of gestation had no effect on MAO activity in immature male or female offspring. However, MAO activity in adult male offspring of DPH treated dams was almost as high as that in adult females. Subcutaneous injection of 10mg/kg DPH for 5 days did not alter MAO activity in prepubertal or postpubertal rats of either sex. Thus, prenatal administration of DPH can program changes in adult male MAO activity. These changes were not due to diminished levels of testosterone. 45 references. (Author abstract modified)

003975 Ishikawa, T.; Yamamoto, M. Central Research Laboratories, Yamanouchi Pharmaceutical Co. Ltd., Azusawa, Itabashi-ku, Tokyo 174, Japan **Effects of butyrophenone and phenothia-**

zine derivatives on the caudate spindle. Pharmacology. 20(6):316-322, 1980.

The effects of butyrophenone and phenothiazine derivatives on the caudate spindle were examined in gallamine immobilized cats. Butyrophenone derivatives (haloperidol, trifluperidol, and methylperidol) inhibited the caudate spindle activity in a dose related manner by 13.5% to 86.5%. Phenothiazine derivatives (chlorpromazine, perphenazine, and trifluoperazine) inhibited the caudate spindle activity only by 4.0% to 25.1%. These results are discussed in relation to the different CNS effects and clinical effects of the drug derivatives. 19 references. (Author abstract modified)

003976 Ivanova-Chemishanska, L.; Antov, G. Institute of Hygiene and Occupational Health, Medical Academy, Sofia, Bulgaria **Dithiocarbamate Endodan changes activity of brain enzymes in rats.** Activitas Nervosa Superior. 21(4):273-274, 1979.

The influence of dithiocarbamate Endodan on activity of brain enzymes in rats was studied. Endodan was administered orally for 180 days to two groups of albino rats, and at 100 and 180 days, the activity of LDH, SucDH, G6PDH, G1DH, AcP, ATPase, G6Pase, CytOase and the quantity of SH and -S-S-groups as well as soluble proteins were determined in the brain. After 100 days of administration, a statistically significant increase of SucDH and LDH activity, decrease of ATPase activity, and a nonsignificant increase in G6PDH activity were found in the high dose group and decreased ATPase activity in the low dose group. At 180 days, ACP activity increased and the activity of ATPase decreased in both groups. 11 references.

003977 Janka, Z.; Szentistvanyi, I.; Juhasz, A.; Rimanoczy, A. Dept. of Neurology and Psychiatry, University Medical School, Szeged, Hungary **Difference in lithium transport between neurones and glia in primary culture.** Neuropharmacology. 19(9):827-830, 1980.

Measurements of lithium influx and efflux in primary cultures with different proportions of neuronal and glial cells dissociated from chick embryonic brain showed that neuronal cells had higher lithium transport rates and high intracellular lithium levels at steady-state than glial cells. It is suggested that neurons may possess a more active molecular mechanism for transmembrane lithium movement than glia. 17 references. (Author abstract modified)

003978 Javors, Martin; Erwin, V. Gene. School of Pharmacy, University of Colorado, Boulder, CO 80309 **Effects of benzodiazepines and valproic acid on brain aldehyde reductase and a proposed mechanism on anticonvulsant action.** Biochemical Pharmacology. 29(12):1703-1708, 1980.

Benzodiazepines (clonazepam, diazepam, flurazepam, fosazepam, lorazepam, nitrazepam, oxazepam and R07-5202) were shown to inhibit the activity of brain aldehyde reductase obtained from DBA/2J mice with the IC50 values (concentration of inhibitor of 50% of control activity) ranging from 0.24 to 7.0mM ED50. Values of these benzodiazepines for protection against maximal electroshock-induced convulsions were determined for DBA/2J mice which were pretreated with either saline or beta-diethylaminoethyl diphenylpropylacetate (SKF-525-A), an inhibitor of microsomal drug metabolizing systems. Spearman rank order and Person correlation coefficients between the IC50 values for inhibition of aldehyde reductase activity and the ED50 values for protection against maximal electroshock-induced convulsions were calculated to be 0.62 and 0.82, respectively, for a group of eight benzodiazepines. When the animals were pretreated with SKF-525A, the correlation coefficients were 0.83 and 0.71, respectively. Rm values, indicators of relative lipid solubility, were measured for these benzodiazepines. Correlations between Rm values and IC50 values or ED50 values were not significant at the 95% confidence level. Data are consistent with the hypothesis that highly reactive aldehyde intermediates of biogenic amine metabolism may be implicated in anticonvulsant drug action. 34 references. (Author abstract modified)

003979 Jork, R.; Lossner, B.; Matthies, H. Institute of Pharmacology and Toxicology, Medical Academy, 301 Magdeburg, Germany **The influence of dopamine on the incorporation of different sugars into total proteins of hippocampal slices.** Pharmacology Biochemistry and Behavior. 13(2):303-304, 1980.

Dopamine significantly increased the incorporation of L-fucose and D-mannose into total proteins of male Wistar rat hippocampal slices. Dopamine only slightly enhanced the incorporation of D-galactose and N-acetyl-D-glucosamin and had no effect on incorporation of N-acetyl-neuraminic acid. Results suggest that dopamine's effect on glycoprotein formation depends on the kind of nucleotides necessary for activation of sugars and not on the sugar's final position in the glycan chain. 10 references. (Author abstract modified)

003980 Juorio, A. V. Psychiatric Research Division, University Hospital, Saskatoon, Saskatchewan S7N OW8, Canada **Drug-induced changes in the formation, storage and metabolism of tyramine in the mouse.** British Journal of Pharmacology. 66(3):377-384, 1979.

Antipsychotic drugs (chlorpromazine, haloperidol, spiroperidol, alpha-flupenthixol, and d-butaclamol) reduced the concentration of p-tyramine in the striatum of male Swiss mice. These drugs tended to increase striatal concentrations of m-tyramine, but the effect was significant only for haloperidol and d-butaclamol. Antipsychotic drugs significantly reduced striatal p-tyramine in mice pretreated with tranylcypromine or clorgyline, compared with concentrations in mice given only a monoamine oxidase inhibitor. The moderate increase in striatal m-tyramine caused by monoamine oxidase inhibition was not altered by antipsychotic drugs. Drugs that reduce dopamine turnover (apomorphine, piribedil, lergotrile, and alpha-methyl-tyrosine) significantly increased striatal p-tyramine. No significant changes in striatal m-tyramine concentrations were seen after apomorphine, piribedil, or lergotrile, but alpha-methyl-p-tyrosine reduced m-tyramine concentration. Drugs that impair amine storage (reserpine, tetrabenazine, and oxypertine) reduced striatal concentrations of p-tyramine; reserpine and tetrabenazine also reduced m-tyramine concentrations. Results suggest that striatal tyramines may act as modulators in the control of dopaminergic neurons. 48 references. (Author abstract modified)

003981 Jurna, I. Pharmakologisches Institut, Universitat des Saarlandes, D-6650 Homburg/Saar, Germany **Effect of stimulation in the periaqueductal grey matter on activity in ascending axons of the rat spinal cord: selective inhibition of activity evoked by afferent Adelta and C fibre stimulation and failure of naloxone to reduce inhibition.** Brain Research. 196(1):33-42, 1980.

In rats with prenigral decerebration, the effects of electrical stimulation of the periaqueductal grey matter (PAG) on the activity recorded from axons ascending in the spinal cord were investigated. These axons were activated by electrical stimulation of afferent A-beta, A-delta, and C-fibers in the ipsilateral sural nerve. Stimulation of the PAG with trains of impulses by itself evoked ascending activity, but strongly depressed the impulse transmission from C-fibres to neurons with ascending axons. It exerted a weaker effect on impulse transmission from Adeltla fibers and had no effect on impulse transmission from Abeta fibers to neurons with ascending axons. Intravenous naloxone, lmg/kg, did not diminish the depressant effect of PAG stimula-

tion. Intravenous morphine depressed the activation of ascending axons from afferent C-fibers more markedly than that from afferent Adelta fibers, but did not modify the depression of ascending activity produced by PAG stimulation. Naxolone antagonized the depressant effect of morphine. Results indicate that PAG stimulation inhibits ascending activity evoked by noxious stimuli by a mechanism which does not necessarily involve endogenous opiates. 37 references. (Author abstract modified)

003982 Kalivas, Peter W.; Halpern, Lawrence M.; Horita, Akira. Dept. of Pharmacology, School of Medicine, University of Washington, Seattle, WA 98195 **Synchronization of hippocampal and cortical electroencephalogram by thyrotropin-releasing hormone.** Experimental Neurology. 69(3):627-638, 1980.

The synchronization of hippocampal and cortical EEG by thyrotropin-releasing hormone (TRH) is described. It is noted that the septal region has recently been shown to be extremely sensitive to TRH-induced antagonism of pentobarbital narcosis in the rat. As the septohippocampal system is thought to provide a neuroanatomical substrate mediating synchronization of the hippocampal EEG, it was hypothesized that TRH would induce hippocampal synchrony. Animals were pretreated with pentobarbital and both hippocampal and cortical EEG monitored. By using spectral analysis of the EEG, it was shown that intracerebroventricular administration of TRH caused a significant increase in both hippocampal (3 to 7 Hz) and cortical (7 to 11 Hz) synchrony. It is postulated that TRH-induced hippocampal synchrony may play a role in TRH antagonism of pentobarbital narcosis. 29 references. (Author abstract modified)

003983 Kan, J. P.; Benedetti, M. Strolin. Centre de Recherche Delalande, 10 rue des Carrieres, F-92500 Rueil-Malmaison, France **Antagonism between long acting monoamine oxidase inhibitors (MAOI) and MD780515, a new specific and reversible MAOI.** Life Sciences. 26(25):2165-2171, 1980.

The inhibition of type-A and type-B monoamine oxidase (MAO-A, MAO-B) in rat brain, liver, and heart by MD780515, was investigated ex vivo with 5-hydroxytryptamine (5-HT) and betaphenylethylamine (PEA) as substrates. MAO-A was strongly inhibited for 4 hours after oral administration of MD780515. The strong inhibition of MAO-A remaining in the three tissues 24 hr after oral administrtion of clorgyline was completely removed by pretreatment with MD780515. In the same conditions, MD780515 against the inhibition by clorgyline of PEA deamination in heart. Inhibition of brain MAO-B by tranylcypromine was not modified by pretreatment with oral doses of MD780515. Results are consistent with a specific and reversible inhibition of MAO-A acitivity by MD780515 which can protect against long acting MAO-A inhibitory effects of clorgyline and tranylcypromine. MD780515 enhances the selectivity of tranylcypromine. 30 references. (Author abstract modified)

003984 Kandasamy, S. B. College of Pharmacy, 644 NE, 14th, University of Oklahoma Health Sciences Center, Oklahoma City, OK 73190 **Central effect of dibutyryl cyclic AMP on the temperature in the conscious rabbit.** Pharmacology. 20(6):304-309, 1980.

In the rabbit, intracerebroventricular administration of dibutyryl cyclic AMP (DBC) produces fever which was selectively antagonized by phenoxybenzamine, indicating the involvement of central alpha-adrenoceptors in DBC-induced fever. The decrease in DBC hyperthermia after 6-hydroxydopamine (6-OHDA) supports the view that DBC-induced fever is dependent on the presence of noradrenaline (NA) in the CNS. The accentuation of NA hyperthermia by theophylline suggests that NA fever may be mediated by cyclic AMP. It is considered unlikely that DBC-induced hyperthermia in the rabbit is mediated via prostaglandins since indomethacin does not inhibit this response to DBC. 13 references. (Author abstract)

003985 Kandel, Stephen I.; Steinberg, Glenn H.; Wells, James W.; Kandel, Marianne; Gornall, Allan G. Faculty of Pharmacy, University of Toronto, Toronto, Ontario, Canada M5S 1A1 **Separate binding sites for histaminic drugs in rat cerebral cortex.** Biochemical Pharmacology. 29(16):2269-2272, 1980.

The binding of (3H)mepyramine, (3H)histamine, and (3H)cimetidine in the same subcellular fraction of rat cerebral cortex was investigated to probe the relationships among the receptor sites for these radiolabelled drugs. Results describe a paradox wherein agreement between binding affinity and H2 pharmacological potency occurs at one site for H2 antagonists and at a separate and mutually independent site for H2 agonists. No interconversion of these sites has been observed under the conditions of the binding studies. While this pattern appears to argue in favor of separate sites for agonists and antagonists in controlling H2 responses in vivo, it must be noted that a correlation does not in itself establish that a binding site is indeed a receptor. 14 references.

003986 Kant, G. Jean; Muller, Thomas W.; Lenox, Robert H.; Meyerhoff, James L. Dept. of Medical Neurosciences, Division of Neuropsychiatry, Walter Reed Army Institute of Research, Washington, DC 20012 **In vivo effects of pentobarbital and halothane anesthesia on levels of adenosine 3',5'-monophosphate and guanosine 3',5'-monophosphate in rat brain regions and pituitary.** Biochemical Pharmacology. 29(13):1891-1896, 1980.

The effects of two general anesthetics, pentobarbital and halothane, on in vivo levels of cyclic AMP and cyclic GMP were examined in 17 brain regions and the pituitary in the rat. Ventilation was controlled to produce normal values of arterial pH, pCO2, and pO2, to eliminate changes in cerebral perfusion and oxygen delivery which occur as a result of the respiratory depressant effect of these drugs. Arterial pressure was monitored and colonic temperature was maintained within normal limits. Pentobarbital was given as a single i.p. injection of 80mg/kg. After 3 min in a jar flushed with 3% halothane in air, the Ss received 2% halothane in air via a nose cone, and were killed by microwave irradiation 1 h after the start of anesthesia. Both drugs decreased levels of cyclic GMP in virtually all regions. The largest changes occurred in the cerebellum, where cyclic GMP dropped to 7.4% of control with pentobarbital and to 9.8% of control following halothane. Levels of cyclic AMP significantly increased in the cerebellum, brainstem, and hypothalamus after halothane, by 58%, 49%, and 65%, respectfully. Both pentobarbital and halothane markedly increased cyclic AMP levels in the pituitary to (784% and 270% of control values, respectively). These results show that halothane and pentobarbital, which modify synaptic transmission, selectively alter cyclic AMP and cyclic GMP levels in specific brain regions and the pituitary. 32 references. (Author abstract modified)

003987 Kimura, Kiyoshi; Kimura, Yutaka; Ohata, Katsuya: Takagi, Hiroshi. Nippon Shinyaku Research Laboratories, Kyoto 601, Japan **Effects of intraventricularly administered serotonin, noradrenaline, dopamine and metaraminol on the reserpine-induced spikes recorded from the medial nucleus trapezoides in rabbits.** Japanese Journal of Pharmacology. 29(1):33-39, 1979.

The effects of intraventricular administration of 30 or 50mcg of serotonin (5-HT), noradrenaline (NA), dopamine (DA), and metaraminol on the reserpine-induced spikes recorded from the medial nucleus trapezoides of male rabbits were investigated. NA and 5-HT both produced marked decreases in amplitude and discharge rates of the spikes within minutes of administration, but DA had no significant effects. Metaraminol, a metabo-

lite of alpha-methyl-m-tyrosine, produced potent suppression of spikes, with gradual onset and long duration of action; the spikes were completely suppressed 90 minutes after administration and no recovery was observed within 6 hours. 12 references. (Author abstract modified)

003988 Kinoshita, Fumiko; Nakai, Yoshikatsu; Katakami, Hideki; Kato, Yuzuru; Yajima, Haruaki; Imura, Hiroo. Second Division, Dept. of Internal Medicine, Faculty of Medicine, Kyoto University, Kyoto 606, Japan **Effect of beta-endorphin on pulsatile luteinizing hormone release in conscious castrated rats.** Life Sciences. 27(10):843-846, 1980.

Injection of 1mcg of beta-endorphine into the lateral ventricle of castrated conscious Wistar rats inhibited the pulsatile discharge of luteinizing hormone (LH). Intravenous administration of naloxone antagonized this effect. It is suggested that beta-endorphin acts on central opiate receptors to inhibit LH release. 9 references. (Author abstract modified)

003989 Kirksey, D. F.; Slotkin, T. A. Grosvenor Hall, College of Osteopathic Medicine, Ohio University, Athens,)OH 45701 **Concomitant development of (3H)-dopamine and (3H)-5-hydroxytryptamine uptake systems in rat brain regions.** British Journal of Pharmacology. 67(3):387-391, 1979.

The synaptosomal uptake of 5-hydroxytryptamine (5-HT) and dopamine (DA) was examined in the cerebral cortex, corpus striatum, and midbrain plus brainstem of developing Sprague-Dawley rats. A parallel, biphasic development of the 5-HT and DA uptake systems was observed in all regions examined; the most rapid increases occurred in the first 2 weeks of life, followed by a slower rate of increases the next 3 to 4 weeks. Kinetic studies indicated that the developmental increases in transmitter uptake reflect changes in the numbers of terminals rather than in the affinities of the uptake systems. The similarity in the maturational patterns of the two systems suggests that a common ontogenetic event or series of events may trigger the outgrowth of both 5-HT and DA neurons. 19 references. (Author abstract modified)

003990 Klemm, William R.; Mallari, Clinton G. Dept. of Biology, Texas A&M University, College Station, TX **Effects of morphine and naloxone on the responsiveness (unit and field potential) of three opiate-relevant brain areas during electrical stimulation of the substantia nigra.** Progress in Neuro-Psychopharmacology. 4(1):1-12, 1980.

The effects of morphine and naloxone on the responsiveness (unit and field potential) of three opiate-relevant brain areas during electrical stimulation of the substantia nigra were investigated in 27 paralyzed and unanesthetized rats. During pretreatment, unit activity usually increased during 1/sec electrical stimulation of the substantia nigra in the three brain areas tested (central grey, amygdala, and caudate). Morphine generally depressed the evoked increases in unit activity in all areas. However, morphine enhanced evoked activity in a significant number of caudate and amygdala loci. In the central grey, depression was more distinct and consistent. The administration of naloxone after morphine generally reversed the unit and field potential depressed, but reversal was less consistent in the caudate. In neural populations where morphine enhanced unit activity, naloxone had no clear effect. 27 references. (Author abstract modified)

003991 Knowles, W. Douglas; Phillips, M. Ian. Phillips: Dept of Physiology and Biophysics, University of Iowa, Iowa City, IA 52242 **Angiotensin II responsive cells in the organum vasculosum lamina terminalis (OVLT) recorded in hypothalamic brain slices.** Brain Research. 197(1):256-259, 1980.

The responses of cells in the organum vasculosum lamina terminalis (OVLT) to angiotensin II (AII) were recorded in hypothalamic brain slices, uncontaminated by input from other brain regions, physiological variables, and anesthetic effects. Thirty-two cells in the OVLT region were tested with iontophoretic injection of AII in brain slices from nine rats. The rates of firing of the cells were compared for approximately 20 sec periods before and during injection. The majority of the neurons recorded in the region of the OVLT are specifically excited by iontophoretic applications of AII. 13 references.

003992 Koelle, George B,; Rickard, Kathleen Kitto; Smyrl, Eloise Gabel. Dept. of Pharmacology, Medical School/G3, University of Pennsylvania, Philadelphia, PA 19104 **Steady state and regenerating levels of acetylcholinesterase in the superior cervical ganglion of the rat following selective inactivation of propionylcholinesterase.** Journal of Neurochemistry. 33(6):1159-1164, 1979.

The effects of selective inactivation of propionylcholinesterase (PrChE) by tetramonoisopropylprophosphortetramide (iso-OMPA) on the steady-state and regenerating levels of acetylcholinesterase (AChE) were investigated on the superior cervical ganglion (SLG) of the rat. Over the dosage range of 1.5 to 40.mcM 150-OMPA/Kg intraperitoneally, which produced nearly total inactivation of ganglionic PrChE and 0% to 35% inactivation of AChE, there was no subsequent increase in AChE activity above the control level. Single or repeated injections of iso-OMPA at total doses of 5.0 to 40.0mcM/kg intraperitoneally caused no reduction in the rate of regeneration of ganglionic AChE during the 24 hours following its inactivation by sarin, 2.0mcM/kg intravenously. Both sets of findings differ from those obtained previously in a similar study of ganglionic AChE and butyrlcholinesterase (BuChE) in the cat. Possible reasons for this distinct species differences are discussed. 18 references. (Author abstract)

003993 Koide, T.; Uyemura, K. Dept. of Pharmacology, Research Laboratories of Chigai Pharmaceutical Co. Ltd. No. 41-8, 3-chome, Takada, Toshima-ku, Tokyo, Japan **Preferential inhibition of type B-MAO by new compounds, 1-(3-(dimethylamino)propyl) 5 methyl-3-phenyl-1H-indazole (FS32) and its N-desmethylated derivative (FS97).** Neuropharmacology. 19(9):871-875, 1980.

Two new compounds, 1-(3-(dimethylamino)propyl)-5-methyl-3-phenyl-1H-indazole (FS32) and its N-desmethylated derivative (FS97), preferentially inhibited the type-B form of monoamine oxidase (MAO) in a mitochondrial fraction prepared from whole rat brain. Type-B MAO was also more susceptible than type-A MAO to inhibition by classical tricyclic antidepressants. Kinetic studies showed that FS32 and FS97 are both competitive and reversible inhibitors of type-A and type-B MAO. 31 references. (Author abstract modified)

003994 Kolchinskaya, L. I.; Lishko, V. K.; Barchenko, L. I. Institut fiziologii im. A. A. Bogomol'tsa AN, Ukrainskoy SSR, Kiev, USSR /Studies on interaction of p-nitrophenylphosphate with Na, K-ATPase./ **Izucheniye vzaimodeystviya n-nitrofenilfosfata s Na, K-ATPazoy.** Ukrainskyi Biokhimicheskiy Zhurnal. 51(3):211-217, 1979.

The vector characteristics of the interact Na, K-ATPase and ouabaine were studied in experiments on the restored ghosts of erythrocytes. It was shown that the effect of K on the enzyme activity was the same when ATP or p-nitrophenylphosphate (p-NPP) was the phosphorylating agent. ADP removed the p-NPP-induced inhibition with ouabaine. This effect was explained by the addition of ADP to the enzyme substrate. Incorporation of labelled orthophosphate into p-nitrophenol (NP) in

the presence of Na, K-ATPase preparations was not detected. It was shown that antibodies against the fraction of the brain microsomes inhibit K-NPPases to a lesser extent than Na, K-ATPase. Digitonin treatment did not remove (Na ATP) in the K-NPPase activity. It is concluded that the mechanism of p-NPP hydrolysis differs from the mechanism of ATP hydrolysis. 26 references. (Journal abstract modified)

003995 Korczyn, Amos D.; Eshel, Yechiel; Keren, Ora. Dept. of Physiology and Pharmacology, Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Israel **Enkephalin mydriasis in mice.** European Journal of Pharmacology. 65(2/3):285-287, 1980.

Met-enkephalin, leu-enkephalin, and D-Ala-D-leu-enkephalin produced mydriasis in male ICR mice, but none was as potent as morphine. Naloxone antagonized the effects of all agents to a similar extent. Since naloxone and D-phenylalanine had no direct effect on pupillary size, it is concluded that the enkephalins are probably not involved in the physiological regulation of pupillary diameter. However, testing for mydriasis may provide a simple method for screening drugs for effects on central opiate receptors. 8 references. (Author abstract modified)

003996 Koss, Michael C. Dept. of Pharmacology, University of Oklahoma, Health Sciences Center, P. O. Box 26901, Oklahoma City, OK 73190 **Clonidine mydriasis in the cat: further evidence for a CNS postsynaptic action.** Naunyn-Schmiedeberg's Archives of Pharmacology. 309(3):235-239, 1979.

Clonidine (1 to 100mcg/kg i.v.) and d-amphetamine (500mcg, intracerebroventricularly) produced mydriasis associated with depression of tonic ciliary nerve activity in the anesthetized cat. Amine depletion by reserpine and alpha-methyl-p-tyrosine did not alter the effects of clonidine, but totally prevented the amphetamine-induced mydriasis and parasympathetic nerve depression. Pretreatment with yohimbine (0.5mg/kg i.v.) totally blocked the effects of both drugs. Results suggest that the pupillary dilation induced by i.v. clonidine and central amphetamine is due to central inhibition of parasympathetic tone to the iris. Clonidine appears to produce this effect by acting on postsynaptic mechanisms, while amphetamine acts indirectly through release of an endogenous inhibitory transmitter. The yohimbine antagonism of the effects of both drugs suggests that a central adrenergic inhibitory mechanism is involved. 31 references. (Author abstract modified)

003997 Kouyoumdjian, J. C.; Gonnard, P.; Belin, M. F. Gonnard: Dept. de Biochimie, C.H.U. Henri-Mondor, Universite Paris XII, F-94010 Creteil, France **Effect of fenfluramine administration on synaptosomal uptake of some neurotransmitters and on synaptosomal enzymes which metabolise GABA.** Naunyn-Schmiedeberg's Archives of Pharmacology. 309(1):7-11, 1979.

Fenfluramine reduced synaptosomal uptake of 5-hydroxytryptamine (5-HT), GABA, and glutamic acid (Glu) in male Sprague-Dawley rat brain synaptosomes. The inhibition was competive for 5-HT and noncompetitive for GABA and Glu. Fenfluramine also increased glutamic acid decarboxylase activity and decreased GABA-transaminase activity in synapotosomes. 15 references. (Author abstract modified)

003998 Kozik, M. B. Dept. of Neuropathology, AM, Przybyszewskiego 49, 60-355 Poznam, Poland **The effect of ZnC12 ingestion on the activity of various phosphatases and esterases of the rat brain.** Activitas Nervosa Superior. 21(4):277-278, 1979.

The effect of ZnC12 ingestion on the activity of various phosphatases and esterases of the rat brain was studied. Wistar rats were treated intragastrically with a daily dose of 50mg ZnC12 over a period of 21 days, and the effects of this treatment on the activity of the following enzymes of the brain were examined. It was found that: 1) intragastrical administration of ZnC12 over a period of 21 days caused degeneration and necrosis of nerve cells along with hyperplasia of theoligodendroglia; 2) rats ingesting ZnC12 for a period of 21 days showed increased levels of cerebral TPPase and acP activities, along with depletion of the cerebral AChE and ATPase activities; and 3) the activity of NsE, ChE, and AlkP were unaffected by chronic ZnC12 intoxication. 6 references.

003999 Kuhn, Donald M.; Meyer, Mary Anne; Lovenberg, Walter. Section of Biochemical Pharmacology, NHLBI, NIH, Bethesda, MD 20205 **Activation of rat brain tryptophan hydroxylase by polyelectrolytes.** Biochemical Pharmacology. 28(22):3255-3260, 1979.

The in vitro activity of male Sprague-Dawley rat brain tryptophan hydroxylase was increased twofold by heparin and fourfold by dextran sulfate. The enzyme activity was not altered by the polysaccharides dermatan sulfate, hyaluronic acid, and chondroitin sulfate, or by the unsulfated polymer dextran. A variety of polyanions (including DNA, glycogen, poly-d-gulutamic acid, and poly-l-glutamic acid) had no effect on tryptophan hydroxylase, but salts (sodium chloride, potassium chloride, magnesium sulfate, and ammonium sulfate) inhibited the enzyme, indicating the effects of heparin and dextran sulfate on tryptophan hydroxylase were not mediated by increases in ionic strength perse. Several lines of evidence suggested that tryptophan hydroxylase binds ionically to these polyelectrolytes. It is suggested that the binding of certain polyelectrolytes to tryptophan hydroxylase may induce a conformational change in the enzyme that results in increased catalytic activity. 22 references. (Author abstract modified)

0004000 Laduron, P. M.; Janssen, P. F. M. Dept. of Biochemical Pharmacology, Janssen Pharmaceutica, B-2340 Beerse, Belgium **Characterization and subcellular localization of brain muscarinic receptors labelled in vivo by (3H) dexetimide.** Journal of Neurochemistry. 33(6):1223-1231, 1979.

The characterization and subcellular localization of brain muscarinic receptors labelled in vivo by (3H) dexetimide is described. Following i.v. injection of labelled drug into rats, radioactivity specifically accumulates in brain regions containing muscarinic receptors but not in cerebellum. This accumulation is stereospecific, saturable and displaceable by unlabelled desetimide. In contrast, (3H) levetimide, the inactive enantiomer, does not show such preferential uptake or stereospecific displacement. An analytical approach was used to study the subcellular distribution of (3H) dexetimide binding sites. After differential centrifugation, the binding sites are mainly recovered in the microsomal fraction from different brain regions but not from the cerebellum. After displacement, the radioactivity is found in the supernatant. After equilibration in a density gradient the distribution pattern of (3H)dexetimide is biomodal, like that of 5'-nucleotidase, with a major peak in a region of low density. When the microsomal fraction was treated with digitonin, three groups of membrane were characterized by isopycnic centrifugation on the basis of their differential shift to higher densities. Evidence is provided that the postsynaptic membranes bearing muscarinic receptors belong to the class of plasma membranes. Finally, digitonin treatment may represent a useful tool to produce subfractions enriched in postsynaptic membranes which can now be identified biochemically in binding experiments. 34 references. (Author abstract)

0004001 Lange, David G.; Fujimoto, James M.; Fuhrman-Lane, Carolyn L.; Wang, Richard I. H. P. O. Box 26509, Dept. of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, WI 53226 **Unidirectional non-cross tolerance to etor-**

phine in morphine-tolerant mice and role of the blood-brain barrier. Toxicology and Applied Pharmacology. 54(2):177-186, 1980.

A unidirectional noncross-tolerance phenomenon to etorphine was observed under conditions of maximal tolerance development to morphine. Using a morphine pellet implantation technique, a 30 fold increase in the analgesic ED50 for subcutaneously (sc) administered morphine was observed. When 30 fold morphine tolerant animals were examined for cross-tolerance to sc etorpine, no change in etorphine's analgesic ED50 was observed. The removal of the tolerance inducing morphine pellet prior to analgesia testing resulted in the expression of cross-tolerance to etorphine. Further characterization of the phenomenon was provided by the reverse experiment in which a large amount of cross-tolerance to sc morphine but little tolerance to sc etorphine was observed after etorphine pellet implantation. No change occurred in the analgesic ED50 for intracerebroventricular (icv) administration of etorphine or morphine after the animals were implanted with morphine pellets. These observations implicate the blood-brain barrier as a probable site for the differential expression of narcotic tolerance. 23 references. (Author abstract)

0004002 Law, Ping-Yee; Fischer, Gunther; Loh, Horace H.; Herz, Albert. Dept. of Pharmacology, University of California, San Francisco, CA 91413 **Inhibition of specific opiate binding to synaptic membrane by cerebroside sulfatase.** Biochemical Pharmacology. 28(17):2557-2562, 1979.

The role of cerebroside sulfate in the specific binding of opiates to the Sprague-Dawley synaptic membrane was examined. The hydrolysis of membrane sulfatides by sulfatase-A (cerebroside sulfatase) was dependent on the presence of a heat stable protein molecule. Sulfatase-A attenuated the specific binding of tritiated naloxone, this inhibition was dependent on the concentration of the activator molecule and could not be prevented by the addition of bovine serum albumin in the binding assay mixtures. The enzymatic pH optimum for inhibiting the specific opiate binding (pH 4.7 to 6 5.0) was consistent with the Ph optimum for sulfatase hydrolysis of free cerebroside sulfate molecules. Scatchard analysis indicated a significant decrease in the number of binding sites with no statisitically significant alteration in binding affinity. 22 references. (Author abstract modified)

0004003 Lenicque, P. M.; Wepierre, J.; Cohen, Y. Laboratoire de Pharmacodynamie, Faculte de Pharmacie Paris-Sud, F-92290 Chatenay-Malabry, France **Protection by 4-amino-hex-5-enoic acid (gamma-vinyl GABA) and hypobaric hypoxia against kainic acid neurotoxicity.** Psychopharmacology. 66(1):51-53, 1979.

The behavioral effects of i.p. injections of kainic acid (KA) were compared to those produced by direct local application of KA to brain tissue, and the reduction of these effects by increasing endogenous levels of GABA via hypobaric hypoxia or 4-amino-hex-5-enoic acid (gamma-vinyl GABA) was investigated. The behavioral effects following i.p. injection of KA in rats could be cancelled with hypobaric hypoxia (8% 02, corresponding to 7000m altitude) or with i.p. injections of gamma-vinyl GABA. This protection may result from increased accumulations of GABA in brain tissues. 7 references. (Author abstract modified)

0004004 Lenox, Robert H.; Kant, G. Jean; Meyerhoff, James L. Dept. of Psychiatry, Neuroscience Research Unit, University of Vermont College of Medicine, Burlington, VT 05405 **Regional sensitivity of cyclic AMP and cyclic GMP in rat brain to central cholinergic stimulation.** Life Sciences. 26(25):2201-2209, 1980.

Cyclic AMP and cylcic GMP levels in 18 regions of rat brain were determined following administration of two different centrally active cholinergic agonists, oxotremorine and physostigmine. Administration of oxotremorine, a muscarinic agonist, 10 min prior to sacrifice by exposuire to high power microwave irradiation resulted in significant increases in cyclic GMP in cerebellum, brainstem, hippocampus, midbrain, thalamus, and septal region. Cyclic AMP levels were significantly elevated in substantia nigra, nucleus interpeduncularis, hypothalamus, brainstem, midbrain, and in the pituitary where a greater than 10 fold increase was observed. Levels of plasma prolactin and corticosterone did not differ in any of the groups examined, but growth hormone was significantly lower in animals exposed to oxotremorine. Physostigmine, a cholinesterase inhibitor, administered ip also produced elevations in cyclic AMP and cyclic GMP in several of the brain regions examined. These results indicate that multiple regions of the brain are responsive to central cholinergic activation of not only cyclic GMP, but also cyclic AMP systems. 32 references. (Author abstract modified)

0004005 Lerner, Pauline; Major, L. F.; Dendel, P. S.; Campbell, I. C.; Murphy, D. L. Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Central and peripheral dopamine beta hydroxylase: responses to long term treatment with monoamine oxidase inhibitors.** Neuropharmacology. 19(9):877-881, 1980.

Long-term (3 weeks) treatment with the monoamine oxidase inhibitors clorgyline and pargyline did not alter brain dopamine-beta-hydroxylase (DBH) activity in cats. However, both drugs decreased plasma DBH after 8 days of treatment and decreased cerebrospinal fluid (CSF) DBH after 22 days. The delayed decrease in DBH activity in CSF may be related to the delayed onset of therapeutic effect characteristic of these drugs. 25 references. (Author abstract modified)

0004006 Lichtenwalner, Mark Richard. Temple University **Factors responsible for the longevity of action of phencyclidine. (Ph.D. dissertation).** Dissertation Abstracts International. 40(5):2147-B, 1979. Ann Arbor, Univ. Microfilms No. 7924004, 119p., 1979.

Hypotheses to account for the longevity of action of phencyclidine (PCP) were experimentally addressed both in vitro and in vivo using the mouse and dog. The ionization constant and partition coefficient of PCP were established. Distribution of PCP was studied in the dog at a dose of 1mg/kg intravenously. Relative activities of the metabolites were examined by studying their median lethal doses in mice and their effects on the central nervous activity of mice as measured with the rotarod and the actophotometer. Results showed that the metabolites did have central nervous activity, but that their duration and potency were much reduced from that of PCP. The pharmacokinetics of PCP were examined by analyzing the urine of mice receiving 50mg/kg of PCP and it was found that the rates of elimination of the metabolites were more rapid than their rate of formation. (Journal abstract modified)

0004007 Lin, M. T.; Wang, H. C.; Chandra, A. Dept. of Physiology and Biophysics, National Defense Medical Center, Taipei, Taiwan, China **The effects on thermoregulation of intracerebroventricular injections of acetylcholine, pilocarpine, physostigmine, atropine and hemicholinium in the rat.** Neuropharmacology. 19(6):561-565, 1980.

The effects of intracerebroventricular (icv) injections of acetylcholine, pilocarpine, physostigmine, atropine, and hemicholinium on the thermoregulatory functions of rats to ambient temperatures (Ta) of 8 and 22 degrees Celsius were assessed. Intracerebroventricular injections of acetylcholine, pilocarpine, and physostigmine each produced a dose dependent hypother-

mia in rats at both 8 and 22 degrees. The hypothermia in response to either acetylcholine, pilocarpine or physostigmine was brought about by both decreased metabolic heat production and cutaneous vasodilatation. Furthermore, the hypothermia induced by these agents was greatly reduced by pretreatment of animals with a small dose of atropine. In addition, icv injection of a larger dose of atropine and hemicholinium each produced a dose dependent hypothermia at both Ta of 8 and 22 degrees. The hypothermia in response to atropine and hemicholinium was brought about solely by a reduction in metabolic heat production. Thus in the rat, icv injection of acetylcholine, pilocarpine, physostigmine, atropine and hemicholinium each produce the hypothermic effects, and icv injection of atropine (2 micrograms; which had no effects on rectal temperature at this dose) blocks the hypothermic effects induced by acetylcholine pilocarpine and physostigmine in the rat. 23 references. (Author abstract modified)

0004008 Lin, M. T., Chern, Y. F.; Wang, Zyx; Wang, H. S. Dept. of Physiology and Biophysics, National Defence Medical Center, Taipei, Taiwan, China **Effects of apomorphine on thermoregulatory responses of rats to different ambient temperatures.** Canadian Journal of Physiology and Pharmacology. 57(5):469-475, 1979.

Systemically or centrally administered apomorphine produced dose related decreases in rectal temperature in male Sprague-Dawley rats at ambient temperatures (Ta) of 8 C. and 22 degrees, At 8 degrees, the hypothermia was brought about by a decrease in metabolic rate (M), but at 22 degrees the hypothermia was due to an increase in mean skin temperature, an increase in respiratory evaporative heat loss (Eres), and a decrease in M. At a Ta of 29 degrees, apomorphine increased rectal temperatures, due to increased M and decreased Eres. The hypothermic and hyperthermic effects of apomorphine were antagonized by haloperidol or 6-hyrdoxydopamine, but not by 5,6-dihydroxytryptamine. Results indicate that apomorphine acts on dopamine neurons within the brain, with both presynaptic and postsynaptic sites of action, to influence body temperatures. 22 references. (Author abstract modified)

0004009 List, Stephen; Titeler, Milt; Seeman, Philip. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 1A8 **High-affinity 3H-dopamine receptors (d3 sites) in human and rat brain.** Biochemical Pharmacology. 29(11):1621-1622, 1980.

The characterization of high affinity 3H-dopamine binding in rat and human brains is presented, and the ability to compete with specific binding of 3H-dopamine of a variety of drugs was evaluated. The data indicate that the high affinity dopamine site labelled by 3H-dopamine in the rat and human brain is similar to the extensively studied high affinity dopamine receptors labelled by 3H-dopamine in the calf. Since this high affinity dopamine receptor has now been shown to have a high affinity for dopaminergic agonists, to have a dopaminergic distribution, and to be present in three separate species, it is proposed that this receptor be called the D3 dopamine receptor. 5 references.

0004010 Logan, J. G.; O'Donovan, D. J. Dept. of Physiology, London Hospital Medical College, Turner Street, London E-1 2AD, England **Noradrenaline uptake by synaptosomes and (Na-K) ATPase.** Biochemical Pharmacology. 29(15):2105-2112, 1980.

The uptake of (3H)noradrenaline (NA) by synaptosomes prepared from rat cerebral cortex and brainstem was studied. Results indicate that there are two distinct systems for the uptake of noradrenaline. One system which predominates in cortical tissue has a sodium dependent maximum rate of transport. This uptake system has a number of characteristics which are similar to the synaptic membrane (Na-K) adenosine triphosphatase (ATPase). The activity of this enzyme was studied and the influence of a number of amines determined. Serotonin, tyrosine, L-dopa, dopamine, NA, and adrenaline were all stimulants of the (Na-K) ATPase. Fenfluramines, phentolamine, chlorpromazine, and desipramine antagonized the amine stimulation of (Na-K) ATPase. Desipramine, which was a more potent inhibitor of NA uptake than was chlorpromazine, was less effective than chlorpromazine as an antagonist of the amine stumulation of (Na-K) ATPase. Although there was some similarity between the NA uptake system and the NA stimulated (Na-K) ATPase, these results do not support the contention that synaptosomal uptake of NA is a primary active transport process. 30 references. (Author abstract modified)

0004011 Loonen, Anton J. M.; Soudijn, Willem; van Rooij, Hans H.; van Wijngaarden, Ineke. Dept. of Pharmaceutical Chemistry, University of Amsterdam, Plantage Muidergracht 24, NL-1018 TV Amsterdam, The Netherlands **The regional localization of R28935 in the cat brain as dependent on the route of administration.** Naunyn-Schmiedeberg's Archives of Pharmacology. 309(1):281-285, 1979.

The regional distribution of the antihypertensive agent R28935 and its pharmacologically less active threo-isomer R29814 in cat brain after i.v. injection differed from that observed after administration via the left vertebral artery. Levels were almost equal in all parts of the brain after i.v. administration, levels of both compounds were higher in caudal structures than in rostral structures after injection into the vertebral artery. Differences in concentrations in homotopic brain areas were observed, particulary in the brainstem. The two isomers had the same physicochemical properties, but R28935 penetrated more readily than R29814 into the CNS. It is suggested that the mesencephalic tegmentum, nucleus of the solitary tract, inferior colliculi, and locus coeruleus are possible sites of the hypotensive action of R28935. 13 references. (Author abstract modified)

0004012 Lyness, W. H.; Demarest, K. T.; Moore, K. E. Dept. of Pharmacology and Toxicology, Michigan State University, East Lansing, MI 48824 **Effects of d-amphetamine and disruption of 5-hydroxytryptaminergic neuronal systems on the synthesis of dopamine in selected regions of the rat brain.** Neuropharmacology. 19(9):883-889, 1980.

In male Sprague-Dawley rats, d-amphetamine (0.5 to 2mg/kg i.p.) caused a marked increase in dopamine (DA) syntehsis in striatum, a modest increase in olfactory tubercle, and no change in nucleus accumbens or median eminence. At the highest dose, d-amphetamine slightly reduced DA synthesis in substantia nigra. Depletion of 5-hydroxytryptamine with an intracerebroventricular injection of 5,7-dihydroxytryptamine (5,7-DHT) or a systemic injection of p-chlorophenylalanine (pCPA) enhanced spontaneous and amphetamine stimulated locomotor activity. Pretreatment with 5,7-DHT did not alter DA synthesis in any brain region tested in animals injected with d-amphetamine or its vehicle. Pretreatment with pCPA reduced DA synthesis only in regions containing terminals of mesolimbic DA nerves. 39 references. (Author abstract modified)

0004013 Lyness, W. H.; Friedle, N. M.; Moore, K. E. Dept. of Pharmacology and Toxicology, Michigan State University, East Lansing, MI 48824 **Increased self-administration of d-amphetamine after destruction of 5-hydroxytryptaminergic neurons.** Pharmacology Biochemistry and Behavior. 12(6):937-941, 1980.

Increased self-administration of d-amphetamine after destruction of 5-hydroxytryptaminergic neurons is reported. Animals injected intraventricularly with 5,7-dihydroxytryptamine, which selectively destroys 5-hydroxytryptamine containing neurons,

consistently self-injected larger amounts of d-amphetamine from the first day of training, but the acquisition of a stable rate of drug self-administration was not altered. Bilateral microinjection of 5,7-dihydroxytryptamine into nucleus accumbens failed to alter either the acquisition of d-amphetamine self-administration or the maintenance of a stable rate of injection. 19 references. (Author abstract modified)

0004014 MacMillan, V. Dept. of Medicine, Room 7214, Medical Sciences Building, University of Toronto, Toronto, Ontario, Canada M5A 1A8 **A comparison of the effects of gamma-hydroxybutyrate and gamma-butyrolactone on cerebral carbohydrate metabolism.** Canadian Journal of Physiology and Pharmacology. 57(8):787-797, 1979.

The metabolic effects of 60 minute exposure to gamma-hydroxybutyrate (GHB, 250 to 2000mg/kg) or gamma-butyrolactone (GBL, 150 to 1200mg/kg) were studied in male Wistar rats by measuring cerebral hemispheric levels of energy phosphates and glycolytic/Krebs' cycle metabolites. A general pattern increased glycogen and glucose with decreased pyruvate, lactate, alpha-ketoglutarate, and malate was observed. In association with unchanged adenylates and decreased energy phosphate utilization, this pattern suggested metabolic adaptation to a state of central cerebral depression. The major qualitative difference between the two drugs was that higher doses of GBL were associated with additional decreases of citrate and glutamate secondary to hypercapnia. GHB and GBL were not associated with consistent alterations of the cytoplasmic redox state. 36 references. (Author abstract modified)

0004015 MacMillan, V. Dept. of Medicine, University of Toronto, Medical Sciences Building, Toronto, Ontario, Canada M5S 1A8 **The effects of the anticonvulsant valproic acid on cerebral indole amine metabolism.** Canadian Journal of Physiology and Pharmacology. 57(8):843-847, 1979.

One hour after i.p. administration of 500mg/kg valproic acid to male Wistar rats, cerebral levels of tryptophan and 5-hydroxyindoleacetic acid (5-HIAA) were increased, but 5-hydroxytryptophan (5-HTP) and 5-hydroxytraptamine (5-HT) were unchanged. Valproic acid did not alter levels of 5-HTP or DOPA in rats pretreated with the decarboxylase inhibitor 3-hydroxybenzylhydrazine, 5-HT or dopamine levels in animals pretreated with the monoamine oxidase inhibitor pargyline, or 5-HIAA levels in rats pretreated with probenecid. Results suggest that valproic acid does not alter the rate of tryptophan hydroxylation or the synthesis of 5-HT, but does inhibit the transport mechanism that removes 5-HIAA from the brain. 21 references. (Author abstract modified)

0004016 Maj, J.; Lewandowska, A.; Rawtow, A. Instytut farmakologii AN, ul. Smetnej 12, 31-343 Karkow, Poland **Central antiserotonin action of amitriptyline.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(3):281-285, 1979.

To determine whether amitriptyline (AMI) has a central antiserotonin activity previously demonstrated for doxepin, AMI was administered to rats and mice. Results show that AMI at low doses antagonized the head twitch response to L-5-hydroxytryptophan or 5-methoxytryptamine, as well as tryptamine-induced convulsions. In the limb flexor reflex preparation of the spinal rat AMI acted as a serotonin antagonist. When administered alone, it did not change the flexor reflex but prevented its stimulation induced by serotoninmimetics, not affecting the one evoked by noradrenalinemimetics. At higher doses AMI revealed a noradrenolytic activity. Results indicate that AMI has a central antiserotonin activity similar to that of doxepin. 25 references. (Author abstract modified)

0004017 Makman, Maynard H.; Dvorkin, Bernyce; Horowitz, Sara G.; Thal, Leon J. Dept. of Biochemistry, Molecular Pharmacology and Neurology, Albert Einstein College of Medicine, Bronx, NY 10461 **Retina contains guanine nucleotide sensitive and insensitive classes of dopamine receptors.** European Journal of Pharmacology. 63(2/3):217-222, 1980.

A study of dopamine receptors in calf and rat retina revealed high affinity, stereospecific, saturable binding sites for 3H-spiroperidol and for 3H-2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene (3H-ADTN). The 3H-ADTN sites could be subdivided into two discrete classes, one sensitive to guanine nucleotide inhibition and the other insensitive to guanine nucleotides. The binding of agonists to the 3H-spiroperidol sites was also inhibited by guanine nucleotides. 10 references. (Author abstract modified)

0004018 Manberg, P. J.; Nemeroff, C. B.; Prange, A. J., Jr. Dept. of Psychiatry, Biological Sciences Research Center, University of North Carolina, Chapel Hill, NC 27514 **Thyrotropin-releasing hormone and amphetamine: a comparison of pharmacological profiles in animals. (Unpublished paper).** Research Report, NIMH Grant MH-32316, 1979. 12 p.

Effects produced by thyrotropin-releasing hormone (TRH) and those produced by d-amphetamine were examined in three areas: 1) direct behavioral effects; 2) interaction with other pharmacological agents; and 3) effects on acknowledged neurotransmitter systems. Both TRH and d-amphetamine are shown to exert a wide range of behavioral and biochemical effects. It is noted that the data reviewed would be more helpful in identifying the mode or modes of action for TRH if the comparison substance, d-amphetamine, had a single or only a few cellular actions. One or more of the d-amphetamine actions on the part of TRH may account for the behavioral similarities that it bears to amphetamine. On the other hand, TRH probably exerts cellular actions not exerted by amphetamine, for each has distinctive as well as shared behavioral properties. It is shown that it is impossible to propose a single mechanism of action to explain the behavioral effects of TRH. 65 references. (Author abstract modified)

0004019 Margalit, D.; Segal, M. Isotope Dept. Weizmann Institute of Science, Rehovot, Israel. **A pharmacologic study of analgesia produced by stimulation of the nucleus locus coeruleus.** Psychopharmacology. 62(2):169-173, 1979.

Pharmacologic studies of analgesia produced by stimulation of the nucleus locus coeruleus (LC) were conducted using the rat hot plate test. A correlation between self-stimulation and analgesia produced by stimulation of LC was found. Analgesia produced by LC stimulation was attenuated by naloxone, a morphine antagonist, cyproheptidine, a serotonin antagonist, and WB-4101, an alpha-adrenergic antagonist. The analgesia was absent in 6-hydroxydopamine treated rats. Catecholamine synthesis inhibition by a combination of reserpine and AMT or more specific inhibition of noradrenaline synthesis by DDC elevated latency to paw lick and yet did not affect stimulation produced analgesia. It is suggested that morphinergic, serotonergic, and alpha-adrenergic mechanisms mediate LC stimulation produced analgesia. 17 references. (Author abstract)

0004020 Marshall, Kenneth C.; Murray, J. Scott. Dept. of Physiology, University of Ottawa, Ottawa, Ontario, Canada K1N 9A9 **Cholinergic facilitation of thalamic relay transmission in the cat.** Experimental Neurology. 69(2):318-333, 1980.

The effects of intravenously injected atropine and physostigmine were tested on field potentials evoked in ventral anterior and ventral lateral, ventral posterolateral, and lateral geniculate nuclei of the thalamus by electrical stimulation of principal af-

ferent pathways. Postsynaptic components of potentials evoked by stimulation of the brachium conjunctivum, medial lemniscus, and optic tract were usually selectively enhanced by physostigmine and depressed by atropine. Responses evoked in the ventral nucleus by stimulation of the precruciate cortex were similarly altered, but in a smaller proportion of tests. In a small number of tests, the nicotinic blocker, mecamylamine, was also found to depress the postsynaptic responses to stimulation of the three major afferent pathways. Transmission in these pathways and the effects of drug administrations were partly dependent on the anesthetic state of the animal. Halothane and pentobarbital administration depressed the postsynaptic responses. It is possible that depression of thalamic relay transmission by anesthetic agents, by anticholinergic drugs, and during slow-wave sleep may all reflect interaction with a common cholinergic neuronal system. 35 references. (Author abstract)

0004021 Martin, John R.; Quock, Raymond M. Dept. of Pharmacology, School of Medicine, University of Minnesota, Minneapolis, MN 55455 **Differential sensitivity of spontaneously hypertensive rats to the hypothermic effect of dopaminergic drugs.** Life Sciences. 27(3):253-258, 1980.

The differential sensitivity of spontaneously hypertensive rats to the hypothermic effect of dopaminergic drugs was investigated. It was found that the dopaminergic agonist apomorphine produces dose related hypothermia in naive rats as does L-DOPA in carbidopapretreated rats. The hypothermic responses to these two dopaminergic drugs were significantly more pronounced and prolonged in the spontaneously hypertensive rat than in normotensive Wistar control rats. The greater sensitivity of the spontaneously hypertensive rat to these drugs was reflected as a leftward shift of the dose response curves of apomorpine and L-DOPA-induced hypothermias. 13 references. (Author abstract modified)

0004022 Martin, M. R. Building 36, Room 5D 32, LNO, NINCDS, NIH, Bethesda, MD 20205 **The effects of iontophoretically applied antagonists on auditory nerve and amino acid evoked excitation of anteroventral cochlear nucleus neurons.** Neuropharmacology. 19(6):519-528, 1980.

The actions of glutamine diethylester (GDEE) were compared with those of D-alpha-aminoadipate (DAA), DL-alpha-aminosuberate (DLAS), HA-966 and magnesium (Mg) ions on glutamate, aspartate and N-methyl-D-aspartate (NMDA)-induced excitation of cat anteroventral cochlear nucleus neurons and on the synaptic excitation by the auditory nerve. GDEE consistently depressed glutamate, more than aspartate responses and had little if any effect on NMDA responses and synaptic transmission. The responses to NMDA and aspartate were particularly sensitive to DAA, DLAS, and Mg ions. The synaptically evoked response was also sensitive to DAA, DLAS, and Mg ions as well as HA-966. Results indicate that the synaptic receptor is of the NMDA type. Although a transmitter role for glutamate in a folded configuration is not ruled out, the preferential interaction of aspartate with the synaptic receptor suggests that aspartate is more likely to be the transmitter in the auditory nerve. 27 references. (Author abstract modified)

0004023 Mason, Michael Francis. University of Health Sciences/Chicago Medical School **Beta-phenylethylamine: factors regulating its concentration and distribution in blood. (Ph.D. dissertation).** Dissertation Abstracts International. 40(6):2630-B, 1979. Ann Arbor, Univ. Microfilms No. 7926673, 141p., 1979.

The normative blood level and factors regulating concentration and distribution of phenylethylamine (PEA), an endogenous amine which may regulate affective behavior, was investigated using the rabbit as an experimental model. A series of separate in vitro experiments indicated that PEA, and probably amphetamine, enter the rabbit erythrocyte via lipid solubility mediated diffusion with a smaller component of Na dependent, ouabain sensitive, carrier mediated facilitated diffusion. The source of energy for this accumulation is probably the Na/K gradient. Less than 2% of the PEA is bound to erythrocyte membrane. The binding of PEA to plasma proteins, although measured indirectly, is approximately 18%. Phenylacetic acid, the main metabolite of PEA, distributed as expected from its degree of ionization at the pH of the incubation medium (T/M=90). The similarities exhibited in uptake and transport of numerous compounds at the membranes of the blood-brain barrier and erythrocyte enabled the postulation of a rabbit erythrocyte model for the study of uptake and transport mechanisms at the blood-brain barrier. An erythrocyte uptake index could be of value for drug uptake and transport at the blood-brain barrier; and discrepancies/similarities in predicted/experimental values could aid in characterization or discovery of new and distinct transport systems. (Journal abstract modified)

0004024 Massotti, M.; Guidotti, A. FDA, Bureau of Drugs, Division of Drug Biology, 200 C St. SW, Washington, DC 20204 **Endogenous regulators of benzodiazepine recognition sites.** Life Sciences. 27(10):847-854, 1980.

Data for 3H-diazepam binding and GABA-induced stimulation of 3H-diazepam binding to crude rat synaptic membranes varied with the method used to prepare the membranes. The changes in 3H-diazepam binding, triggered by occupancy of GABA recognition sites, appeared to be mediated by endogenous membrane factors that decrease the number of high affinity binding sites for GABA and reduced the affinity of the benzodiazepine recognition sites for 3H-diazepam. It may be necessary to completely remove GABA or the endogenous inhibitors from membranes to study the intrinsic characteristics of compounds that act as ligands for benzodiazepine binding sites. 10 references. (Author abstract modified)

0004025 Mayer, Joel M.; Khanna, Jatinder M.; Kalant, Harold; Spero, Lawrence. Dept. of Pharmacology, University of Toronto, Toronto, Canada M5S 1A8 **Cross-tolerance between ethanol and morphine in the guinea-pig ileum longitudinal-muscle/myenteric plexus preparation.** European Journal of Pharmacology. 63(2/3):223-227, 1980.

Tolerance to the inhibitory effects of morphine and cross-tolerance to those of ethanol were demonstrated in the guinea-pig iLeum longitudinal muscle/myenteric plexus preparation in vivo (morphinization with implanted morphine pellets) and in vitro (18 hour incubation with morphine). Daily ethanol injections resulted in tolerance to ethanol and cross-tolerance to morphine. Results suggest that ethanol and morphine have similar actions on this preparation. 11 references. (Author abstract modified)

0004026 Maziarz, L. J. Dept. of Neuropathology, AM, Przybyszewskiego 49, 60-355 Poznan, Poland **Morphological and histochemical changes in the Ammon's horn and the cortex of cerebellum provoked by intoxication with zinc diethyldithiocarbamate.** Activitas Nervosa Superior. 21(4):280-281, 1979.

Morphological and histochemical changes in the Ammon's horn and the cortex of cerebellum provoked by intoxication with zinc diethyldithiocarbamate were examined. Eighteen adult Wistar rats were fed intragastrically with 1.0g of Cynkotox (zinc diethyldithiocarbamate) for 10 consecutive days, and acid phophatase and acetylcholinesterase activities were studied in brain slices. Cynkotox produced morphological changes of pyramidal cells; cells were shrunken and surrounded by proliferating oligodendroglia. Cynkotox produced relatively little change

within Ammon's horn and cerebellar cortex, however. 4 references.

0004027 Mazurkiewicz-Kwilecki, I. M. Dept. of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada **Propranolol and brain histamine: acute and chronic effects.** General Pharmacology. 10:97-101, 1979.

Evidence is presented that chronic administration of propranolol to rats causes a significant decrease in the hypothalamic and midbrain histamine concentration. No pronounced alterations were noted after acute treatment. Spontaneous locomotor activity was markedly reduced following acute propranolol administration, and a short lasting sedation was still noted 17 hr. after the last chronic drug treatment. Rectal temperature was significantly reduced after acute propranolol treatment, and tolerance to the acute hypothermic effect did not develop with chronic propranolol administration. Results suggest a possible involvement of brain histamine in some of the chronic effects of propranolol. (Journal abstract modified)

0004028 McBride, W. J.; Frederickson, R. C. A. Dept. of Psychiatry, Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, IN 46223 **Taurine as a possible inhibitory transmitter in the cerebellum.** Federation Proceedings. 39(9):2701-2705, 1980.

A series of studies investigating taurine as a possible inhibitory transmitter in the cerebellum is described. Cellular deletion studies indicated that taurine was not present in granule cells but appeared to be present in relatively high amounts in the inhibitory stellate cells as well as the excitatory climbing fibers in the cerebellum of the rat. Microdissection of the cerebellum demonstrated that the content of taurine was significantly higher in the molecular layer than in the granular layer, white matter or deep nuclei. The level of taurine was threefold greater than the level of GABA in the molecular layer and the distribution pattern of taurine among the four cerebellar regions was different than that of GABA. Microiontophoretic application of taurine induced an inhibition of spike discharge in 88% of the Purkinje cells and other cerebellar neurons tested. Taurine appeared to be one half to one fifth as potent as GABA in the cerebellum. The data are consistent with a possible role for taurine as the inhibitory transmitter released from stellate cells. In addition, taurine might serve another, yet unknown, role in the cerebellum, since it appears to be present in the excitatory climbing fibers of the cerebellum. 27 references. (Author abstract modified)

0004029 McCall, Robert B.; Aghajanian, George K. Upjohn Company, Cardiovascular Disease Research, Unit 7243-209-3, Kalamazoo, MI 49001 **Pharmacological characterization of serotonin receptors in the facial motor nucleus: a microiontophoretic study.** European Journal of Pharmacology. 65(2/3):175-183, 1980.

Microiontophoretic application or i.v. injection of methysergide, cyproheptadine, cinanserin, or metergoline antagonized the facilitating effect of serotonin (5HT) on facial motoneuron excitation in rats, but did not alter facilitation induced by norepinephrine (NE). Chronic administration of metergoline results in supersensitivity to 5-HT and NE in the facial nucleus. Chlorpromazine, propranolol, and methiothepin failed to block the facilitating effect of 5-HT, but methiothepin did block the effect of NE. Results are discussed in relation to a two compartment model of the motor syndrome mediated by 5-HT. 37 references. (Author abstract modified)

0004030 McCown, Thomas Jarmon. Vanderbilt University **The development of tolerance to amphetamine reward and blockade by para-chloroamphetamine: a possible role for serotonin? (Ph.D. dissertation).** Dissertation Abstracts International. 40(6):2631-B, 1979. Ann Arbor, Univ. Microfilms No. 7926616, 153p., 1979.

The development of tolerance to amphetamine reward and blockade by para-chloroamphetamine (PCA) were examined in the rat. After a chronic AMP injection regimen, all animals increased the amount of self-administered AMP by at least 45% compared to baseline, indicating tolerance development. No differences found between chronic AMP and saline treated rats, so that tolerance did not result from metabolic changes. Preferential dopamine (DA) reduction in rats prepared for self-administration caused an increase in drug intake, indicating that the reward value of self-administered AMP had been diminished. Norepinephrine reduction did not change AMP self-administration from pretreatment baseline. Data show that dopaminergic activity mediated the expression of AMP reward. Pretreatment with PCA, which selectively depletes serotonin (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA), prior to the chronic injection regimen resulted in no tolerance development to self-administered AMP, suggesting that 5-HT activity mediates tolerance to AMP. Neither chronic AMP alone nor in combination with PCA changed 5-HT or 5-HIAA levels in discrete brain regions. An additional series of experiments failed to corroborate serotonergic involvement in the development of AMP tolerance. Thus, PCA blockade mechanisms remain unclear. As acute AMP caused an apparent increase in serotonergic transmission, it is speculated that tolerance might result from a combination of inhibitory serotonergic input and chronic AMP-induced changes in either presynaptic or postsynaptic DA function. (Journal abstract modified)

0004031 McDermott, Lois J.; Grossman, Sebastian P. Grossman: Dept. of Behavioral Sciences, University of Chicago, 5848 S. University Ave., Chicago, IL 60637 **The effects of amphetamine or caffeine on the response to glucoprivation in rats with rostral zona incerta lesions.** Pharmacology Biochemistry and Behavior. 12(6):949-957, 1980.

Lesions in the rostral zona incerta (ZI) of male albino rats were found to severely impair feeding responses to 2-deoxy-D-glucose (2DG) and drinking responses to hypertonic saline during the first month after surgery. There was evidence of recovery 6 months after surgery but the magnitude of the improvement was small and severe impairments persisted in most Ss. A small but significant deficit in the feeding response to insulin persisted unabated after the 6 month recovery period. Caffeine or amphetamine pretreatment, but not apomorphine, increased ad lib feeding as well as the response to low doses of 2DG in rats with ZI lesions as well as in controls. The increased feeding response to 2DG after caffeine or amphetamine was larger than the sum of the effects of 2DG alone plus the effect of caffeine or amphetamine alone. 38 references. (Author abstract)

0004032 McIntyre, Dan C. Dept. of Psychology, Carleton University, Ottawa, Ontario K1S 5B6, Canada **Amygdala kindling in rats: facilitation after local amygdala norepinephrine depletion with 6-hydroxydopamine.** Experimental Neurology. 69(2):395-407, 1980.

Rats with bilateral amygdala electrodes were pretreated by local injection of 6-hydroxydopamine (6OH) into the amygdala. In different groups, the 6OH was applied either bilaterally or unilaterally. If unilateral, the 6OH was administered either to the first kindled amygdala site or the second kindled, contralateral amygdala site. The 6OH depleted the amygdala of norepinephrine and resulted in a reduction in the number of stimulations required to kindle convulsions. This facilitation was observed only from the 6OH treated kindled sites and was insignificant after 6OH treatment of the contralateral site. There was

no effect of 6OH on measures of convulsion performance (latency and duration) or after discharge duration. These data have implications in terms of a proposed model of amygdala kindling in the rat. 39 references. (Author abstract)

0004033 Memo, M.; Lucchi, L.; Spano, P. F.; Trabucchi, M. Dept. of Pharmacology and Pharmacognosy, University of Milan, Milan, Italy **Lack of correlation between the neurochemical and behavioral effects induced by d-amphetamine in chronically lead-treated rats.** Neuropharmacology. 19(8):795-799, 1980.

D-amphetamine increased locomotor activity in normal Sprague-Dawley rats, but not in those chronically exposed to lead. Biochemical changes induced by d-amphetamine in the central dopaminergic system were identical in the lead treated and control rats. Results indicate that the motor activity elicited by d-amphetamine cannot be correlated with dopaminergic function in rats chronically treated with lead. 13 references. (Author abstract modified)

0004034 Menkes, David B.; Aghajanian, George K.; McCall, Robert B. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Chronic antidepressant treatment enhances alpha-adrenergic and serotonergic responses in the facial nucleus.** Life Sciences. 27(1):45-55, 1980.

The responsiveness of rat facial motoneurons to norepinephrine (NE) and serotonin (5-HT) was assessed with single unit recording and microiontophoretic techniques. Treatment of rats with daily intraperitoneal injections of severely clinically effective tricyclics for 14 to 20 days was found to enhance responses to NE, 5-HT, and to an intravenously administered 5-HT agonist, 5-methoxy-N,N-dimethyltryptamine (5-MeODMT). These changes in sensitivity were not seen in animals chronically treated with saline, chlorpromazine, or fluoxetine, and thus appear specific to antidepressants. Acute effects of tricyclics on NE and 5-HT responses were variable, dependent on the specific drug tested, and appear to have no necessary relation to the pronounced sensitization produced by chronic treatment. 54 references. (Author abstract modified)

0004035 Menteshashvili, N. P. Institut fiziologii im. I. S. Beritashvili, AN Gruzinskoy, SSR, Tbilisi, USSR /Effect of prolonged loading with lysine on distribution of free amino acids in the brain./ **Vliyaniye prodolzhitel'noy nagruzki lizinom na raspredeleniye svobodykh aminokislot v golovnom mozge.** Ukrainskyi Biokhimicheskiy Zhurnal. 51(3):267-269, 1979.

The effects of prolonged loading with small amounts of lysine on changes in free amino acid distribution in the rat brain were studied. Prolonged loading with lysine and a mixture of lysine and metabolism cofactors was found to evoke considerable shifts in the distribution of the amino acid pool in the rat cerebral cortex. Under the influence of lysine the functional activity of the central nervous system improved. 13 references. (Journal abstract modified)

0004036 Meyerson, Laurence R.; Ong, Helen H.; Martin, Lawrence L.; Ellis, Daniel B. Dept. of Central Nervous System Research, Medical Research Division, American Cyanamid Co., Pearl River, NY 10965 **Effect of antidepressant agents on beta-adrenergic receptor and neurotransmitter regulatory systems.** Pharmacology Biochemistry and Behavior. 12(6):943-948, 1980.

The effects of established and novel antidepressant agents on brain monoamine oxidase (MAO) A and B; high affinity synaptosomal uptake of norepinephrine, dopamine, and serotonin; and beta-adrengergic receptor kinetics evaluated by (3H)-dihydroalprenolol binding to cortical membranes are described. Extremely weak in vitro inhibitory effects on rat brain mitochondrial MAO-A and MAO-B were observed with P74-1197 and HP-505, both 3-aryl-spiroisobenzofuranpiperidines, P77-2984, a 3-aryl-spirobenzothiophenepiperidine derivative, LM-5008, an indolylethylpiperidine, desipramine, nisoxetine, and P76-2543, a 4-aryl-1,3 benzodiazepine. The kinetics of (3H)-dihydroalprenolol binding were also studied following chronic administration of these same drugs. After 10 days of treatment, heterogeneous results were obtained in that some compounds elicited changes in receptor density and dissociation constant while others, such as nisoxetine, produced no kinetic alterations. While present biochemical antidepressant tests utilized here are designed to evaluate modulations of aminergic systems in terms of neurotransmitter availability, fluxes in concentration and attendant receptor recognition site sensitivities, the underlying mode(s) of action at the cellular level still require further clarification. 44 references. (Author abstract modified)

0004037 Misra, Chandra H.; Shelat, Harnath S.; Smith, Robert C. Section of Behavioral Neurochemistry, Texas Research Institute of Mental Sciences, 1300 Moursund, Texas Medical Center, Houston, TX 77030 **Effect of age on adrenergic and dopaminergic receptor binding in rat brain.** Life Sciences. 27(6):521-526, 1980.

The effects of age on receptor binding of adrenergic and dopaminergic ligands were studied in rat cerebral cortex and striatum, respectively. Compared to rats 5 months of age, 25-month-old rats had a significant decrease in specific binding of the beta-adrenergic antagonist ligand 3H-dihydroalprenolol (DHA), the alpha-adrenergic ligand 3H-WB-4101 in cortex, and the dopaminergic antagonist 3H-spiperone in striatum. Scatchard analysis of ligand binding indicated that the decrease in specific binding was due to a decrease in the number of receptors and not to a change in the affinity of the ligand for the receptor. 16 references. (Author abstract)

0004038 Mobley, Philip L.; Sulser, Fridolin. Vanderbilt University of School of Medicine, Nashville, TN 37217 **Adrenal steroids affect the norepinephrine-sensitive adenylate cyclase system in the rat limbic forebrain.** European Journal of Pharmacology. 65(2/3):321-322, 1980.

The cyclic AMP response to norepinephrine (NE) was significantly enhanced in male Sprague-Dawley rats given bilateral adrenalectomies, compared to those given sham operations. This effect was due to increased maximal responsiveness of the system rather than to altered affinity for NE. No significant changes were seen in basal levels of cyclic AMP. The cyclic AMP response to NE was not enhanced in animals given bilateral demedullation or in those treated with corticosterone for 5 days prior to sacrifice. Corticosterone did not alter the cyclic AMP response to NE in sham operated animals. 5 references.

0004039 Mogilnicka, Ewa; Arbilla, Sonia; Depoortere, Henri; Langer, Salomon Z. Dept. of Biology, Synthelabo, LERS, 58 rue de la Glaciere, F-75013 Paris, France **Rapid eye-movement sleep deprivation decreases the density of 3H-dihydroalprenolol and 3H-imipramine binding sites in the rat cerebral cortex.** European Journal of Pharmacology. 65(2/3):289-292, 1980.

High affinity bindings sites for tritiated imipramine (3H-IMI) and dihydroalprenolol (3H-DHA) in the male Sprague-Dawley rat cerebral cortex were studied after 24, 48, and 72 hours of REM sleep deprivation. Binding was not altered by 24 or 48 hours of REM deprivation, but maximal binding capacities for 3H-IMI and 3H-DHA were significantly reduced and apparent binding affinities were increased after 72 hours of REM deprivation. The reduction in high affinity 3H-IMI and 3H-DHA binding sites observed after 72 hours of REM sleep deprivation may be related to the antidepressant effects of REM sleep deprivation in humans. 10 references. (Author abstract modified)

0004040 Morita, Yoshio; Shinkuma, Denji; Shibagaki, Nobuko. Department of Neurology and Psychiatry, Medical University of Hyogo, Hyogo-ken, Japan **Effects of benzodiazepines on amygdaloid kindled convulsion -- differences of efficacy among diazepam, bromazepam and lorazepam.** Psychiatria et Neurologia Japonica. 81(8):559-564, 1979.

Using an experimental model of kindled convulsion, efficacy of bromazepam and lorazepam was studied in comparison with that of diazepam. Sixteen SD male rats served as models for experimental temporal lobe epilepsy simulating partial seizure secondarily generalized. Electrical stimulation was given to Ss 1 hour after injecting diazepam, bromazepam and lorazepam, when intercellular concentration is the highest, and 2 hours after injection, and motor behavior and EEG were observed, recorded and compared. EEG was evaluated in terms of after discharge (AD) duration; motor behavior was evaluated in terms of five progressive stages (S1-S5). In the case of diazepam and bromazepam at 1 hour after injection, all Ss were inhibited to S1, while in the case of lorazepam five out of seven cases stayed at S1 and two stayed at S2. AD duration does not change much with diazepam, while it decreases remarkably with bromazepam and lorazepam. The findings suggest that the most efficacious compound was bromazepam, followed by lorazepam, followed by diazepam. 15 references.

0004041 Mosnaim, A. D.; Silkaitis, R.; Wolf, M. E. Dept. of Pharmacology, University of Health Sciences/Chicago Medical School, Chicago, IL 60612 **Rabbit brain metabolism of phenylethylamine and tyramine: drug effects.** Life Sciences. 27(7):557-566, 1980.

The effects of a variety of drugs on rabbit brain metabolism of phenylethylamine and tyramine were investigated. Varying amounts of labeled phenylethylamine (PEA), p-tyramine (TRM) and phenylacetic acid (PAAc) were recovered from rabbit brain homogenates at different intervals after the intraventricular administration of either labeled L-phenylalanine or PEA. Previous administration of imipramine or amphetamine decreased the recoveries of PEA and PAAc. Imipramine increased the recovery of TRM, which was not affected by amphetamine. These studies further show the existence of an in vivo brain metabolic pathway linking L-phenylalanine to PEA and TRM. They also indicate that these pathways are modified by a number of centrally active drugs. 37 references. (Author abstract modified)

0004042 Muehlethaler, M.; Gaehwiler, B. H.; Dreifuss, J. J. Dreifuss: Dept. de Physiologie, 20 rue de l'Ecole de Medecine, CH-1211 Geneva, Switzerland **Enkephalin-induced inhibition of hypothalamic paraventricular neurons.** Brain Research. 197(1):264-268, 1980.

To ascertain whether hypothalamic paraventricular nucleus (PVN) neurons possess opiate receptors and can therefore respond to locally released enkephalins, stable enkephalin analogues were bath-applied to coronal slices from adult rat hypothalamus while recording spontaneous firing of PVN neurons. The Met-enkephalin analogues FK 33-824 and FW 34-569 caused a 50% reduction of the firing rate, which was antagonized by naloxone. Morphine also inhibited PVN neurons. Results indicate that opiates produce a potent and apparently specific reduction in PVN firing and suggest that enkephalins may regulate posterior pituitary secretion by acting at hypothalamic and neurohypophysial levels. 25 references. (Author abstract modified)

0004043 Mueller, Robert A.; Lundberg, Dag; Breese, George R. Dept. of Anesthesiology, NCMH 204H, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Evidence that respiratory depression by serotonin agonists may be exerted in the central nervous system.** Pharmacology Biochemistry and Behavior. 13(2):247-255, 1980.

Central serotonin receptors were implicated in the control of basal and carbon dioxide stimulated respiration in Sprague-Dawley rats. The serotonergic agonist 5-methoxy-N,N-dimethyltryptamine and the serotonin precursor 5-hydroxytryptophan decreased tidal volume and minute volume in a dose dependent manner and produced respiratory acidosis. The serotonin antagonist methysergide antagonized this respiratory depressant effect and stimulated respiration when given alone. 31 references. (Author abstract modified)

0004044 Mukherji, Biswanath; Suemaru, Kohso; Sakai, Noboru; Ghosh, Amal K.; Sloviter, Henry A. Harrison Dept. of Surgical Research, School of Medicine, University of Pennsylvania, Philadelphia, PA 19104 **Effects of morphine and methadone on the isolated perfused rat brain.** Biochemical Pharmacology. 29(11):1608-1611, 1980.

The effects of morphine and methadone on the isolated perfused rat brain were investigated. Perfusion of an isolated rat brain preparation with fluid containing morphine caused increases in both glucose consumption and lactate production; perfusion with methadone caused an increase in glucose consumption but no significant increase in lactate production. After perfusion with morphine for 40 min, the concentrations in cerebral tissue of creatine phosphate, adenosine 5'-triphosphate (ATP), glucose and glycogen were decreased and those of lactate and several glycolytic intermediates and the lactate/pyruvate ratio were increased. After perfusion with methadone for 40 min, there was only a small decrease in ATP concentration in cerebral tissue and the lactate pyruvate ratio was increased but to a much lesser degree than in the brains perfused with morphine. Results suggest that morphine may inhibit mitochondrial oxidative activity. 21 references.

0004045 Murakami, N.; Sakata, Y. Dept. of Physiology, Yamaguchi University School of Medicine, Ube, 755, Yamaguchi, Japan **A possible role of the serotonergic system in thermoregulation in the rabbit.** Neuropharmacology. 19(9):891-895, 1980.

Intravenous injection of lysergic acid diethylamide (LSD, 12 to 17mcg/kg) caused hyperthermic responses in male rabbits at ambient temperatures of 15, 25, and 35 degrees C. Direct injections of LSD into the midbrain raphe nuclei also caused an increase in rectal temperature and a fall in ear skin temperature. Heat production increased slightly even at ambient temperatures of 29 degrees after injection of LSD into the nucleus raphe dorsalis, but not after injection into the nucleus raphe magnus. 18 references. (Author abstract modified)

0004046 Napias, C.; Bergman, M. O.; Van Ness, P. C.; Greenlee, D. V.; Olsen, R. W. Division of Biomedical Sciences, University of California, Riverside, CA 92521 **GABA binding in mammalian brain: inhibition by endogenous GABA.** Life Sciences. 27(11):1001-1011, 1980.

Sodium independent binding of GABA to receptor sites in mammalian brain homogenates was much lower in fresh unwashed membranes than in membrane fractions that had been thoroughly washed with buffer or detergent and frozen and thawed several times. The washing procedure removed endogenous inhibitors of GABA binding sites and an increase in GABA binding affinity to a low affinity class of sites. Biochemical characterization of the inhibitor fraction showed that the endogenous inhibitor of GABA binding was GABA itself. 34 references. (Author abstract modified)

0004047 Nehlig, A.; Moncotel, D.; Lehr, P. R. Laboratoire de Physiologie Generale, Universite de Nancy 1 F-54037 Nancy-

Cedex, France **Glutamine synthetase activity in the chick brain during postnatal growth. Effect of MSO.** Life Sciences. 27(6):483-489, 1980.

Glutamine synthetase activity was estimated in the chick cerebral hemispheres, optic lobes, and cerebellum between the first and the 30th day of postnatal growth. Glutamine synthetase activity is higher in the cerebellum than in the cerebral hemispheres and lowest in the optic lobes at 1 day after hatching; at 30 days after hatching, it is the same in the optic lobes and in the cerebellum and lowest in the cerebral hemispheres. The great increase of glutamine synthetase activity between the first and the fourth day after hatching corresponds to the appearance of the heterogenetic of the chick brain glutamate metabolism. The glutamine synthetase activity is inhibited by methionine sulfoximine (MSO) in vivo at values of 87%, 90%, and 89% in cerebral hemispheres, optic lobes and cerebellum of 1,2, and 4-day-old chicks. The enzyme inhibition is less pronounced in vitro and reaches values of about 25% and 75% for 1 and 10nM MSO concentrations, respectively in the three brain areas of the 1 to 4-day-old chick and values slightly lower in the 30-day-chick brain. 22 references. (Author abstract modified)

0004048 Nicoll, R. A.; Alger, B. E.; Jahr, C. E. Dept. of Pharmacology, University of California, San Francisco, CA 94143 **Enkephalin blocks inhibitory pathways in the vertebrate CNS.** Nature. 287(5777):22-25, 1980.

Enkephalin was found to markedly attenuate a variety of GABAergic inhibitory pathways in the CNS, but not to affect the action of GABA. The action of enkephalin is reversed by the specific opiate antagonist, naloxone. Thus, inhibitory interneurons may be primary targets for opioid peptide containing pathways and disinhibition may be of general importance for opioid peptide action in the CNS. It is concluded that the cellular localization of neurotransmitter receptors may be more meaningful than their overall density in determining the relative importance of the neurotransmitter in a particular CNS region. The findings also emphasize the importance of considering transmitter effects in the context of the intrinsic neuronal circuitry of a given CNS region rather than assessing the drug responsiveness of single neurons. 37 references. (Author abstract modified)

0004049 Nielsen-Kudsk, F.; Jakobsen, P. Institute of Pharmacology, University of Aarhus, DK-8000 Aarhus C, Denmark **Disposition pharmacokinetics of lorazepam in the rabbit.** Acta Pharmacologica et Toxicologica. 46(5):388-391, 1980.

The disposition pharmacokinetics of the sedative and anxiolytic drug lorazepam were studied in rabbits after an i.v. bolus injection of 0.3 or 0.6mg. Lorazepam showed distinct linear two compartment characteristics with a mean biological half-life of only 73.7 minutes. The mean half-life of the alpha-phase of distribution was 18.4 minutes, and the mean apparent steady-state volume of distribution was 1.641/kg. The calculated apparent volume of the peripheral compartment was 0.531/kg. These data are compared with lorazepam pharmcokinetics in humans. 11 references. (Author abstract modified)

0004050 Nowycky, Martha C.; Roth, Robert H. Roth: Dept. of Psychiatry, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510 **Chronic gamma-butyrolactone (GBL) treatment: a potential model of dopamine hypoactivity.** Naunyn-Schmiedeberg's Archives of Pharmacology. 309(1):247-254, 1979.

The average firing rates of A9 dopaminergic cells in male Sprague-Dawley Dawley rats were significantly depressed by chronic (1 month) administration of gamma-butyrolactone (GBL) in the drinking water. Striatal dihydroxyphenylacetic acid levels were also depressed, but striatal dopamine levels and tyrosine hydroxylase activity did not differ from control values. Tolerance to the behavioral effects of GBL on righting reflex was observed, but this could be partially overcome by increasing the amount of the challenge dose. The ability of a challenge dose of GBL to elicit increased dopamine synthesis also showed tolerance. Postsynaptic and presynaptic dopamine receptors became supersensitive after chronic treatment with GBL. Results suggest that chronic treatment with GBL may provide a model system for studying the effects of partial deprivation of dopaminegic activity. 29 references. (Author abstract modified)

0004051 Nyback, Henrik; Wiesel, Frits-Axel; Skett, Paul. Laboratory of Experimental Psychiatry, Dept. of Psychiatry, Karolinska Hospital, S-10401 Stockholm, Sweden **Effects of piracetam on brain monoamine metabolism and serum prolactin levels in the rat.** Psychopharmacology. 61(3):235-238, 1979.

The effects of piracetam on brain monoamine metabolism in three regions of rat brain and on serum prolactin levels were investigated. Piracetam, at 5g/kg, i.p., increased the levels of dihydroxyphenylacetic acid, homovanillic acid, and 3-methoxy-4-hydroxyphenylethylene glycol, whereas 5-hydroxyindoleacetic acid was unaffected. The drug also increased prolactin concentrations in serum. The level of dopamine was unchanged in the olfactory tubercle and the striatum. These effects are different from those obtained with amphetamine-like drugs. results indicate that piracetam accelerates brain catecholamine (CA) turnover via a blockade of CA receptors, as suggested for neuroleptic drugs. This effect could be responsible for the therapeutic action of piracetam on psychotic symptoms in psychoorganic disorders of old age. A blockade of brain CA receptors by piracetam is not compatible with facilitated learning which seems to be mediated via other neuron systems than CA pathways. 41 references.

0004052 O'Connor, Michael Francis. University of Nebraska Medical Center **The involvemenn to GABA and cyclic nucleotides in ethanol intoxication and withdrawal. (Ph.D. dissertation).** Dissertation Abstracts International. 40(3):1143-B, 1979. Ann Arbor, Univ. Microfilms No. 7919162, 126p., 1979.

The involvement of gamma-aminobutyric acid (GABA) and the cyclic nucleotides, cAMP and cGMP, in ethanol intoxication and withdrawal was assessed in mice. Cerebellar GABA content was slightly but insignificantly elevated throughout the 4 day intoxication period. Ethanol caused a severe reduction in cGMP concentration at the beginning of the intoxication phase, but tolerance to this effect was established by the end of the period. The concetration of GABA fell during withdrawal to significantly lowered values at 12 and 24 hours of withdrawal. Diazepam was found to nearly obliterate any withdrawal responses when given at the beginning of the withdrawal phase and the increase of cGAMP was also prevented by this dose. (Journal abstract modified)

0004053 Ohnhaus, E. E.; Kirchhof, B.; Peheim, E. Dept. of Medicine, University of Bern, Inselspital, CH-3010 Bern, Switzerland **Effect of enzyme induction on plasma lipids using antipyrine, phenobarbital, and rifampicin.** Clinical Pharmacology and Therapeutics. 25(5, Part 1):591-597, 1979.

Plasma lipids were studied in 19 healthy Ss following induction of the liver microsomal enzyme system by administration of 1200mg antipyrine, 100mg phenobarbital, or 600 or 1200mg rifampicin daily for 14 days. The degree of enzyme induction was greatest after the high dose of rifampicin. D-glucaric acid excretion in urine rose slightly in all groups. Values for gamma-glutamyl-transpeptidase were significantly increased after antipyrine and phenobarbital, but were not altered by rifampicin. The 6-beta-hydroxycortisol urinary excertion corrected by the 17-

hydroxycorticosteroids increased in all groups. No changes in plasma cholesterol, triglyceride, and other plasma concentrations of cholesterol and plasma triglycerides were not elevated after enzyme induction with any of the drugs used. Results suggest that the elevated palsma lipids reported for Ss treated with phenobarbital are not related to enzyme induction by the drug. 31 references. (Author abstract modified)

0004054 Okada, Toshikazu; Seki, Yuhko; Kuruma, Isami. Dept. of Biochemistry, Nippon Roche Research Center, 200-Kajiwara, Kamakura, Kanagawa, Japan **A possible intraneuronal site of action of thymoleptics.** Psychopharmacology. 63(1):67-73, 1979.

The uptake of catecholamines (CAs) into crude mitochondria preparations (P2 fractions) and vesicle preparations from rat hypothalamus and striatum were compared in terms of the inhibition by thymoleptics and other drugs. Thymoleptics preferentially inhibited the uptake of CAs into hypothalamic P2 fractions, while ATPase inhibitors preferentially inhibited the uptake of dopamine into striatal P2 fractions. When the preparation obtained from rats pretreated with reserpine was used, the preferential inhibition of hypothalamic uptake by thymoleptics was entirely abolished. These results indicate that the inhibition of CA uptake by thymoleptics in the hypothalamus is predominantly due to the inhibition at the synaptic vesicle, while in the striatum the uptake at the synaptosomal membrane is predominantly inhibited. 16 references (Author abstract modified)

0004055 Okajima, Taiichiro; Motomatsu, Toshiharu; Kato, Kenichi; Ibayashi, Hiroshi. Third Dept. of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka 8/2, Japan **Naloxone inhibits prolactin and growth hormone release induced by intracellular glucopenia in the rats.** Life Sciences. 27(9):755-760, 1980.

Intraventricular administration of 2-deoxy-D-glucose (2DG), which causes intracellular glucopenia in the CNS, was found to increase plasma prolactin and growth hormone levels in urethane anesthetized male rats. Naloxone, an opiate antagonist, inhibited the 2DG-induced prolactin and growth hormone release. Apomorphine, a dopaminergic agonist, also inhibited the release of these hormones induced by 2DG. These results suggest that endorphins play a role in hypoglycemia-induced prolactin and growth hormone release and that the dopaminergic mechanism may be involved in this phenomenon. 15 references. (Author abstract modified)

0004056 Olesen, Ole Vendelin; Hestbech, Jytte; Thomsen, Klaus. Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Aarhus, Denmark **Potassium reduction of lithium-induced histological changes of the rat kidney.** Toxicology and Applied Pharmacology. 55(1):79-84, 1980.

The effects of a high potassium content in the diet on the development of lithium-induced histological and functional changes of the kidneys were studied in rats. Lithium was administered with the food for periods varying from 3 to 12 weeks in two dose levels leading to serum lithium concentrations of 0.5 to 0.8 and 0.9 to 1.3mmol/liter, respectively. Histological changes were assessed by light microscopy and functional disturbances by determination of water intake and the intake of a 0.46M Nacl solution. Lithium administration led to flattening of the tubular epithelium and widening of the tubular lumens in the distal convoluted tubules and collecting ducts. Focal cortical nephron atrophy and early stages of interstitial fibrosis developed in some rats given lithium for 9 to 12 weeks. Administration of a potassium rich diet reduced the morphological changes in the distal parts of the nephron significantly, most pronounced in the kidneys of rats given the lowest lithium dosage. Potassium also diminished lithium-induced polyuria and the requirement of sodium. Results suggest a general preventive effect of potassium against lithium-induced functional and morphological changes of the kidney. 17 references. (Author abstract modified)

0004057 Oleshansky, M. A. Dept. of Psychiatry, New York University Medical Center, New York, NY 10016 **Inhibition by purine compounds of cyclic GMP-stimulated cyclic AMP phosphodiesterase activity from a particulate fraction of rat striatum.** Life Sciences. 27(12):1089-1095, 1980.

The inhibition of purine compounds of cyclic GMP stimulated cyclic AMP phosphodiesterase activity from a particulate fraction of rat striatum is described. Adenosine inhibited cyclic GMP stimulated cyclic AMP phosphodiesterase activity and basal cyclic AMP phosphodiesterase activity, and blocked cyclic GMP stimulation of cyclic AMP hydrolysis. Inosine and hypoxanthine were found to have a similar profile of action but were less effective. Adenine, guanosine, and guanine blocked cyclic GMP stimulation of cyclic AMP phosphodiesterase activity. These findings suggest a role for physiologically available purine compounds and alkylxanthines in the regulation of cyclic nucleotide metabolism through interaction with cyclic GMP stimulation of cyclic AMP phosphodiesterase activity. 35 references. (Author abstract modified)

0004058 Olpe, Hans-Rudolf; Balcar, Vladimir J.; Bittiger, Helmut; Rink, Hans; Sieber, Peter. Ciba-Geigy Ltd., Pharmaceuticals Division,CH-4002 Basel, Switzerland **Central actions of somatostatin.** European Journal of Pharmacology. 63(2/3):127-133, 1980.

Somatostatin (SRIF) was applied microionotophoretically to neurons in the frontal and parietal neocortex, hippocampus, and striatum of anesthetized male Sprague-Dawley rats. In urethane treated animals, SRIF elicited a dose dependent increase in the firing rate of 74% of neurons tested in the frontal cortex and 46% in the parietal cortex. All cortical cells identified as pyramidal cells were excited. SRIF provoked excitatory responses in 62% of the neurons studied in hippocampus and 81% of neurons tested in the striatu. The magnitude of excitatory responses to SRIF decreased with repeated exposure, indicating desensitization. SRIF did not interfere with the binding of 3H-muscimol to GABA receptor sites and did not alter the release of GABA from preloaded synaptosomes. Results suggest that SRIF produces its excitatory effects directly (by exciting the neuronal membrane) rather than indirectly (by attenuating GABA mediated synaptic inhibition). 18 references. (Author abstract modified)

0004059 Olson, Richard D.; Kastin, Abba J.; Olson, Gayle A.; Coy, David H. Dept. of Psychology, University of New Orleans, New Orleans, LA 70122 **Behavioral effects after systemic injection of opiate peptides.** Psychoneuroendocrinology. 5(1):47-52, 1980.

Research is overviewed on behavioral effects after systemic injection of opiate peptides, demonstrated across a wide range of behaviors in subjects ranging from goldfish to humans. There is evidence that behavioral effects of brain opiates can occur independently of the narcotic effects. Dose response curves for enkephalin and endorphin usually assume an inverted U-shaped function, with 100mcg/kg as the apogee. Use of the peripheral route for administration of opiate peptides has important theoretical and practical implications. 37 references. (Author abstract modified)

0004060 Orzelek-O'Neil, R. M.; Goodman, F. R.; Forney, R. B. Dept. of Toxicology, Indiana University School of Medicine, Indianapolis, IN 46268 **The effects of delta9-tetrahydrocannabinol and nabilone on the isolated guinea pig bronchus.** Toxicology and Applied Pharmacology. 54(3):493-500, 1980.

The direct effects of delta9-tetrahydrocannabinol (THC) and nabilone (Nab), a synthetic cannabinoid, on respiratory smooth muscle was investigated in the isolated guinea-pig bronchus. Neither THC nor Nab influenced the responses of isolated guinea-pig bronchi to carbachol or histamine; therefore, these compounds do not possess antihistaminic or anticholinergic properties in this preparation. The responses to KCl were also unaltered, suggesting that THC or Nab were not altering depolarization. Furthermore, THC or Nab did not alter prostaglandin F2alpha-induced contractile responses of the bronchi, and addition of THC or Nab to submaximally contracted tissues did not cause relaxation. In isolated bronchi obtained from ovalbumin sensitized guinea-pigs, these cannabinoids did not influence the antigen-induced responses of the tissues; hence, these compounds do not appear to be mediator release inhibitors. Thus, it appears that neither of these compounds exert a direct effect on smooth muscle, and that bronchoactivity observed in vivo may be of a nondirect or central origin. 25 references. (Author abstract modified)

0004061 Osterlind, A.; Akesson, A.; Wahlstrom, G. Dept. of Pharmacology, University of Umea, S-90187 Umea, Sweden **Interactions between 1,2-propanediol (propylene glycol) and hexobarbital.** Acta Pharmacologica et Toxicologica. 45(3):245-248, 1979.

The interaction of 1,2-propanediol (propylene glycol) with hexobarbital was studied in male Sprague-Dawley rats using the anesthesia threshold method. The dose needed to obtain a burst suppression of 1 second or more was determined and given as a percent of preexperimental value obtained in the same rat. When the interval between the i.p. injection of 1,2-propanediol (2.06g/kg) and i.v. infusion of hexobarbital was varied from 10 to 50 minutes, the threshold dose for hexobarbital decreased by 13 to 27%. When the interval was fixed at 30 minutes and the dose of 1,2-propanediol was varied, the hexobarbital threshold was significantly decreased after 2.06g/kg 1,2-propanediol but not after 1.03 or 0.52g/kg. With the lowest dose tested (0.25g/kg), a significant increase in hexobarbital threshold occurred, which may correspond to the excitatory effect frequently observed with low doses of CNS depressants such as ethanol. 13 references. (Author abstract modified)

0004062 Paalzow, Gudrun. Dept. of Pharmacology, Pharmaceutical Faculty, University of Uppsala, Biomedical Center, Box 573, S-751 23 Uppsala, Sweden **Naloxone antagonizes theophylline-induced potentiation of morphine inhibition of a nociceptive reaction in rats.** Psychopharmacology. 62(3):235-239, 1979.

The interaction between a low dose of morphine and theophylline was examined in the rat. Theophylline was shown to potentiate the effect of morphine on the threshold for vocalization after withdrawal of stimulation. This response to painful stimulation is considered to be integrated at the level of the thalamus/hypothalamus/rhinencephalon. Naloxone antagonized the effect of the combined treatment with morphine and theophylline, suggesting pharmacological specificity for morphine. The theophylline-induced enhancement of the pharmacological response to morphine was attenuated after pimozide pretreatment, indicating an underlying dopaminergic mechanism. 34 references. (Author abstract modified)

0004063 Parry, Olwen; Roberts, M. H. T. Dept. of Pharmacology, University of Alberta, Edmonton, Alberta, Canada T6G 2H7 **The responses of motoneurones to 5-hydroxytryptamine.** Neuropharmacology. 19(6):515-518, 1980.

The effects of iontophoretically applied 5-hydroxytryptamine (5-HT) on motoneuron field potentials were investigated. Previous reports, using intracellular recording techniques, suggest that 5-HT hyperpolarizes motoneurons. Recording extracellularly, it was found that 5-HT increased the amplitude of the negative component of the motoneuron field potential. An increase in amplitude was interpreted as an increase in the excitability of motoneurons. This was confirmed by the depolarizing agents glutamate and K ions, which also potentiated the negative field potential. Glycine, a substance known to hyperpolarize motoneurons, reduced the field potential. It is suggested that 5-HT depolarizes motoneurons. Since nerve terminals containing 5-HT make intimate contact with motoneurons, a functional role for 5-HT in regulating muscle tone is implicated. 13 references. (Author abstract)

0004064 Pasternak, Gavril W.; Childers, Stephen R.; Snyder, Solomon H. Dept. of Neurology and Pharmacology, Cornell University Medical College, New York, NY 10021 **Opiate analgesia: evidence for mediation by a subpopulation of opiate receptors.** Science. 208(4443):514-516, 1980.

The effects of naloxazone on morphine analgesia were examined by treating mice with naloxone, naloxazone, or saline, giving them various doses of morphine sulfate, and testing them with the tail flick assay; morphine lethality was determined through intraperitoneal injection of high doses of morphine sulfate in groups of mice treated in the same manner. Naloxazone, a hydrazone derivative of the opiate antagonist naloxone, has a high affinity for opiate receptor binding sites. Naloxazone injections reduce opiate receptor binding to extensively washed mouse brain membranes for more than 24 hours, suggesting that the effect is irreversible. High affinity binding sites are abolished by this treatment, whereas low affinity sites are unaffected. Naloxazone treatment blocks the analgesic effects of morphine for at least 24 hours but does not prevent death from high doses of morphine. Thus analgesic but nonlethal opiate effects may be mediated by the high affinity subpopulation of opiate receptors. 10 references. (Author abstract modified)

0004065 Pedata, F.; Sorbi, S.; Pepeu, G. Pepeu: Dept. of Pharmacology, University of Florence, Viale Morgagni 65, I-50134 Florence, Italy **Choline high-affinity uptake and metabolism and choline acetyltransferase activity in the striatum of rats chronically treated with neuroleptics.** Journal of Neurochemistry. 35(3):606-611, 1980.

High affinity uptake of choline and choline acetyltransferase activity (ChAT) were measured in the striatum of rats treated for 45 to 60 days with haloperidol and pimozide daily and with fluspirilene twice a week. Haloperidol and fluspirilene caused a 29%, and pimozide a 38% increase in high affinity uptake of choline. They also caused a significant decrease in ChAT activity: haloperidol, 20%; pimozide, 27%; and fluspirilene, 42%. In rats treated with fluspirilene for 65 to 80 days the metabolism of (3H)choline taken up by striatal synaptosomes was investigated. A 33% increase in total radioactivity, a significant increase in labelled acetylcholine (ACh), a relative decrease in labelled choline, and no change in labelled phosphorylcholine and betaine were found. It is concluded that the increase in high affinity choline uptake caused by chronic administration of neuroleptic drugs is associated with a parallel increase in choline utilization for ACh formation. On the other hand, the decrease in ChAT activity does not appear to influence ACh formation. 29 references. (Author abstract modified)

0004066 Percy, Vivienne A.; Shanley, Brian C. Dept. of Chemical Pathology, University of Stellenbosch, P.O. Box 63, Tygerberg 7505, South Africa **Factors affecting haem degradation in rat brain.** Biochemical Pharmacology. 29(11):1590-1592, 1980.

The rate of haem metabolism in normal mammalian brain and in the brains of animals subjected to treatments known to influ-

ence haem metabolism in liver tissues was compared. Treatment of rats with lead, allylisopropylacetamide, phenobarbitone, or lead in combination with phenobarbitone did not alter the rate of haem degradation in rat brain. However, hepatic haem oxygenase activity was found to be increased approximately 14 fold 16 hr after treatment with lead. Intraperitoneal administration of haem caused a ninefold increase in liver haem oxygenase activity while phenobarbitone was found to be without effect. Results indicate that brain haemoproteins have a low turnover rate, which accords with the data previously obtained with respect to haem biosynthesis. Destabilization of brain haemoproteins could lead to increased brain haem turnover as haem oxygenase is substrate inducible. However, it would appear unlikely that porphyrinogenic agents or lead affect brain haemoprotein function in normal tissue in this way. 19 references.

0004067 Persson, Sven-Ake. Dept. of Pharmacology, University of Umea, S-901 87 Umea, Sweden **Effects of chlorimipramine on the synthesis and metabolism of dopamine in the rat striatum.** Psychopharmacology. 66(1):13-17, 1979.

The effects of chlorimipramine on the synthesis and metabolism of dopamine in rat striatum were investigateed. Chlorimipramine increased the rate of the striatal in vivo tyrosine hydroxylation measured as the accumulation of 3,4-dihydroxphenylalanine (DOPA) after decarboxylase inhibition. The demethylated metabolite of chlorimipramine, desmethylchorimipramine, increased the DOPA accumulation only after oral administration. Chlorimipramine increased the striatal 3,4-dihydroxyphenylacetic acid (DOPAC) levels, while protriptyline had no significant effect. Results indicate that the effects of chlorimipramine on the DOPA accumulation and on the DOPAC levels in the striatum may be mediated directly via central dopamine receptors, but more indirectly via central 5-hydroxytryptaminergic mechanisms. 24 references. (Author abstract modified)

0004068 Peters, David A. V.; Taub, Hillel. Dept. of Pharmacology, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario,Canada **Increased brain 5-hydroxyindole levels in 20-day old rats after administration of haloperidol in the neonatal period.** Research Communications in Psychology, Psychiatry, and Behavior. 5(2):235-238, 1980.

The effects of haloperidol in the neonatal period on brain 5-hydroxyindole levels of Sprague-Dawley rats were examined. When studied at 20 days of age, 5-hydroxytryptamine (5-HT) and 5-hydroxyindole-acetic acid (5-HIAA) levels were significantly increased in cerebellum, medulla, midbrain, pons, temporal cortex, and thalamus with no significant change in seven other brain areas. At 40 days of age 5-hydroxyindole levels did not differ from control values. Results suggest that exposure to haloperidol during the neonatal period may alter the development of central 5-HT containing neurons. 7 references. (Author abstract modified)

0004069 Petersen, Erling N.; Edvinsson, Lars; Hardebo, Jan Erik. Research Laboratories of Ferrosan, Sydmarken 5, DK-2860 Soborg, Denmark **5-HT antagonism on cerebral and common carotid arteries by the 5-HT uptake inhibitors femoxetine and paroxetine.** Acta Pharmacologica et Toxicologica. 45(4):296-301, 1979.

The 5-hydroxytryptamine (5-HT) antagonism of methysergide was compared with that of the phenylpiperidine 5-HT uptake inhibitors, paroxetine and femoxetine. In the isolated cat middle cerebral artery, the 5-HT-induced contractile response was reduced in a noncompetitive fashion by both uptake inhibitors at concentrations above 0.3mcM, which is about 200 times larger than the concentration required for methysergide. In the autoperfused common caritod artery of pithed male Wistar rats, inhibition was observed only at a dose of 5mg/kg i.v. for femoxetine and paroxetine, whereas methysergide totally abolished all 5-HT respones at a dose of 0.001mg/kg. Results indicate that the 5-HT uptake inhibitors femoxetine and paroxetine are weak 5-HT antagonists. 21 references. (Author abstract modified)

0004070 Phillis, J. W.; Bender, A. S.; Wu, P. H. Dept. of Pohysiology, College of Medicine, University of Saskatchewan, Saskatoon, Sask. S7N OWO, Canada **Benzodiazepines inhibit adenosine uptake into rat brain synaptosomes.** Brain Research. 195(2):494-498, 1980.

An inhibitory effect of the benzodiazepines on adenosine uptake by rat brain synaptosomes is described which may be involved in the central actions of the benzodiazepines. Results strongly support the suggestion that the benzodiazepines may exert at least some of their therapeutic actions by enhancing extracellular adenosine levels. The potency of the benzodiazepines as adenosine uptake inhibitors showed a good correlation with their clinical effectiveness. Clonazepam was the most potent of the compounds tested with diazepam, flurazepam, medazepam, bromazepam and chlordiazepoxide being progressively less effective. The close correlation between the ability of the benzodiazepines to inhibit adenosine uptake and their therapeutic potency as anxiolytics, hypnotics, or anticonvulsants suggests that inhibition of adenosine uptake is an important factor in the central action of these compounds. 18 references.

0004071 Phillis, J. W.; Edstrom, J. P.; Ellis, S. W.; Kirkpatrick, J. R. Dept. of Physiology, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Theophylline antagonizes flurazepam-induced depression of cerebral cortical neurons.** Canadian Journal of Physiology and Pharmacology. 57(8):917-920, 1979.

Theophylline (50 to 100mg/kg i.v.) antagonized the depressant actions of adenosine and flurazepam on male Wistar rat cerebral cortical neurons. In light of recent reports that theophylline competes with diazepam for binding sites in brain tissue, this finding suggests that benzodiazepines and adenosines depress central neurons by acting on the same receptors. Alternatively, methyxanthines may be nonspecific antagonists of both adenosines and benzodiazepines or the benzodiazepines may exert their effects by increasing the ambient concentration of adenosine. 12 references. (Author abstract modified)

0004072 Phillis, J. W.; Kirkpatrick, J. R. Dept. of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Actions of various gastrointestinal peptides on the isolated amphibian spinal cord.** Canadian Journal of Physiology and Pharmacology. 57(8):887-899, 1979.

Motilin, substance-P, bombesin, neurotensin, and thyrotropin releasing hormone had potent depolarizing actions on dorsal root terminals and motoneurons in the isolated hemisected toad spinal cord. Adrenocorticotrophic hormone, secretin, and pancreozymin (chloecystokinin) also depolarized root terminals and motoneurons. Leu-enkephalin and met-enkephalin had weak hyperpolarizing actions on the dorsal and ventral root potentials of repetitively stimulated preparations. Gastrin, gastric inhibitory peptide, glucagon, and somatostatin had no apparent effect on the responses in the this preparation. Angiotensin and vasopressin had weak depolarizing effects on the dorsal and ventral roots. Results indicate that many of the peptides common to the gastrointestinal tract and brain have potent excitant actions on neurons of the amphibian spinal cord, suggesting the isolated amphibian spinal cord is a useful preparation for detection of neurally active substances. 76 references. (Author abstract modified)

0004073 Porta, R.; Camardella, M.; Verruti, A.; De Negri, P.; Miele, L.; Pietra, G. Della. Dept. of Biochemistry, 1st Medical School, University of Naples, Naples, Italy **The in vitro inhibition of indoleamine N-methyltransferase by antipsychotic drugs and benzodiazepines.** Research Communications in Psychology, Psychiatry, and Behavior. 5(2):177-184, 1980.

The influence of various psychoactive agents with different pharmacological effects on in vitro indoleamine N-methyltransferase activity was examined. The drugs having a marked anxiolytic activity were found to be inhibitors of the enzyme. Lorazepam and diazepam showed an inhibitory effect of the competitive type with respect to S-adenosylmethionine toward two additional biogenic amine transmethylases, histamine N-methyltransferase, and catechol O-methyltransferase. 19 references. (Author abstract modified)

0004074 Post, Claes; Lewis, David H. Dept. of Clinical Pharmacology, University Hospital, S-58185 Linkoping, Sweden **Displacement of nortriptyline and uptake of 14C-lidocaine in the lung after administration of 14C-lidocaine to nortriptyline intoxicated pigs.** Acta Pharmacologica et Toxicologica. 45(3):218-224, 1979.

The effects of rapid administration of a bolus of lidocaine hydrochloride (2mg/kg) into the right atrium on the displacement of nortriptyline (NT) from the lung of NT intoxicated Swedish land-race pigs were examined. After the 14C-lidocaine bolus, 0.66mcmM NT was displaced from the cardiopulmonary circulation. Lung uptake of 14C-lidocaine during first pass through the lung was not significantly altered by NT. The duration of the QRS complex in the electrocardiogram increased during infusion of NT from 0.07 to 0.14 seconds when 250mg NT had been administered. The QRS duration decreased to 0.09 seconds after injection of 14C-lidocaine. Mean arterial blood pressure and heartrate decreased slightly during infusions of NT but did not change immediately after 14C-lidocaine displaced NT accumulated in the lung and heart and may be useful in treating patients intoxicated with tricyclic antidepressant drugs. 33 references. (Author abstract modified)

0004075 Poupaert, Jacques H.; Adline, Jacques; Claesen, Michel H.; De Laey, Pierre; Dumont, Pierre A. Dept. of Medicinal Chemistry, School of Pharmacy, University of Louvain, B-1200 Brussels, Belgium **Stereochemical aspects of the metabolism of 5-(4'-fluorophenyl)-5-phenylhydantoin in the rat.** Journal of Medicinal Chemistry. 22(9):1140-1142, 1979.

The metabolism of racemic 5-(4'-fluorophenyl)-5-phenylhydantoin was examined in male Wistar rats. The compound differs from the antiepileptic agent 5,5-diphenylhydantoin in that the normal site of hydroxylation in 5,5-diphenylhydantoin is blocked in one of the phenyl groups by a fluorine atom. Following i.p. administration of the 4'-fluoro analogue, (R)-(-)-5-(4'-fluorophenyl)-5-(4'-hydroxyphenyl)hydantoin was identified by gas liquid chromatography/mass spectrometry as a major metabolite in urine. A second metabolite of the catechol type and its corresponding 0-3'-methyl derivative were also detected. 15 references. (Author abstract modified)

0004076 Prange, A. J., Jr.; Nemeroff, C. B.; Bissette, G.; Manberg, P. J.; Osbahr, A. J., III; Burnett, G. B.; Loosen, P. T.; Kraemer, G. W. Biological Sciences Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Neurotensin: distribution of hypothermic response in mammalian and submammalian vertebrates. (Unpublished paper).** Research Report, NIMH Grant MH-32316, 1979. 16 p.

The effects of neurotensin (NT) after central administration in a variety of species were studied to determine the possible physiological role of NT in thermoregulation. Thirteen species, with at least one from each of the vertebrate classes, were selected for study. The data suggest that centrally administered NT exerts a hypothermic effect in mammals except hibernators. A clear exception is the rabbit, in which NT does not cause hypothermia in either the warm or the cold. Species differences in response to cold exposure may explain species differences to responsiveness to NT. The effects of stress on the response to NT were examined to determine whether stress could account for the negative results obtained in some species. The data show that in poikilothermic species NT does not produce a hypothermic effect. 22 references.

0004077 Rabe, Lynn S.; Moreno, L.; Rigor, B. M.; Dafny, N. Dafny: Dept. of Anesthesiology, University of Texas Medical School, Houston, TX 77025 **Effects of halothane on evoked field potentials recorded from cortical and subcortical nuclei.** Neuropharmacology. 19(9):813-825, 1980.

The effects of halothane (0.25, 0.5, 1.0, and 2.0%) on photic and acoustic evoked responses from four brain regions were assessed in freely moving male Sprague-Dawley rats. The average auditory evoked response was more sensitive than the average visual evoked response to halothane; in the auditory cortex, response amplitude increased with small doses and decreased with large doses. Halothane did not alter the early wave of the evoked responses in the sensory relay nuclei (lateral geniculate body and inferior colliculus) but did alter late components. 22 references. (Author abstract modified)

0004078 Raja, Srinivasa N.; Guyenet, Patrice G. Dept. of Anesthesiology, University of Virginia School of Medicine, 1300 Jefferson Park Ave., Charlottesville, VA 22908 **Effects of phencyclidine on the spontaneous activity of monoaminergic neurons.** European Jounal of Pharmacology. 63(2/3):229-233, 1980.

Phencyclidine (PCP, 1.0 to 1.8 mg/kg i.v.) increased the firing rate of a population of slow firing dopaminergic neurons recorded from the substantia nigra of choral hydrate anesthetized male Sprague-Dawley rats. PCP also significantly reduced the potency of d-amphetamine in inhibiting the firing of dopaminergic neurons. The drug produced few changes in the activity of serotonergic neurons in the dorsal raphe but consistently inhibited the firing of noradrenergic neurons in the locus coeruleus. 11 references. (Author abstract)

0004079 Rastogi, R. B.; Singhal, R. L. Singhal: Dept. of Pharmacology, Faculty of Medicine, University of Ottawa, 275 Nicholas St., Ottawa, Ontario K1N 9A9, Canada **Effect of neonatal hypothyroidism and delayed L-triiodothyronine treatment on behavioural activity and norepinephrine and dopamine biosynthetic systems in discrete regions of rat brain.** Psychopharmacology. 62(3):287-293, 1979.

The influence of neonatal hypothyroidism on norepinephrine and dopamine metabolism in certain discrete regions of rat brain was examined. Intraperitoneal administration of 131I to 1-day-old rats significantly impaired the ontogenesis of spontaneous locomotor activity and reduced tyrosine hydroxylase activity in the striatal region. A parallel decrease in norepinephrine levels was observed in hypothalamus, pons-medulla and striatum. Thyroid deficiency in neonatal life also decreased dopamine levels as well as its metabolite, 3,4-dihydroxyphenylacetic acid, in striatal region. Hypothyroidism in young rats increased catechol-0-methyl transferase activity in brainstem, striatum and mid-brain; however, a 40% decline in 0-methylating enzyme was observed in hypothalamus. It is concluded that data suggest that low levels of norepinephrine, dopamine, and their metabolities can be attributed to the decreased synthesis and utilization of these catecholamines in brain. 33 references. (Author abstract modified)

0004080 Raymond, G. G.; DeGennaro, M. D.; Yau, Martin; Buice, Robert G. Buice: University of Tennessee Center for the Health Sciences, Memphis, TN 38163 **Effect of hyperbilirubinemia on the pharmacokinetics of diazepam in the rat.** Research Communications in Chemical Pathology and Pharmacology. 28(1):133-144, 1980.

Diazepam pharmacokinetics were studied in heterozygous (nonjaundiced) and homozygous (jaundiced) male Gunn rats after single i.v. doses of 10mg/kg. Plasma concentration time course data could be described by biexponential equations for both groups. Plasma clearance was faster, elimination half life shorter, and volume of distribution reduced in the jaundiced rats. Results are discussed in relation to the use of diazepam in the treatment of neonatal hyperbilirubinemia. 19 references. (Author abstract modified)

0004081 Redburn, Dianna A.; Chentanez, Thyon. Dept. of Neurobiology and Anatomy, University of Texas Medical School, Houston, TX 77030 **Effect of morphine in vivo on uptake of (3H)-choline and release of (3H)acetylcholine from rat striatal synaptosomes.** Biochemical Pharmacology. 28(19):2961-2966, 1979.

The rates of (3H)choline uptake and (3H)acetylcholine release were measured in male Sprague-Dawley rat striatal synaptosomes in vitro, following in vivo injections of morphine sulfate. Morphine caused a 50% increase in the maximum velocity of (3H)choline uptake and a concomitant increase in (3H)acetylcholine release. It is suggested that morphine has an overall stimulatory effect on the striatal cholinergic system, which may be a transynaptic phenomenon rather than a direct effect on the cholinergic cell. 13 references. (Author abstract modified)

0004082 Redburn, Dianna A.; Clement-Cormier, Yvonne; Lam, Dominic M. K. Dept. of Neurobiology, University of Texas Medical School at Houston, Houston, TX 77030 **Dopamine receptors in the goldfish retina: 3H-spiroperidol and 3H-domperidone binding; and dopamine-stimulated adenylate cyclase activity.** Life Sciences. 27(1):23-31, 1980.

Dopamine receptors in the goldfish retina were examined by binding studies using 3H-spiroperidol and 3H-domperidone as specific ligands, and by measuring retinal adenylate cyclase activities in the presence and absence of dopamine. These results indicate that washed membranes from goldfish retinal homogenate bind a variety of dopamine agonists and antagonists with high affinities and with characteristics similar to those reported for the brain, with the exception that in this retina there is virtually no binding of the specific D2 receptor antagonist, 3H-domperidone. In addition, there is a very low basal activity of adenylate cyclase which can be greatly stimulated by dopamine, possibly reflecting a high degree of coupling between this enzyme and the dopamine receptor. Taken together, these findings indicate that the goldfish retina contains a high density of D1 type dopamine receptors and few, if any, D2 type receptors. 28 references. (Author abstract)

0004083 Reiffenstein, R. J. Dept. of Pharmacology, 9-70 Medical Sciences Building, University of Alberta, Edmonton, Alberta, Canada T6G 2H7 **Release of exogenous gamma-(3H)aminobutyric acid during seizure activity in chronically denervated and normal cat cortex.** Canadian Journal of Physiology and Pharmacology. 57(8):798-803, 1979.

The release of tritiated GABA from normal and chornically denervated cat cortex was studied during seizure activity. When methacholine was used to evoke seizure activity, (3H)GABA release was depressed in both normal and epileptic cortex. Pentylenetetrazol-induced seizures evoked a small increase in (3H)GABA efflux from both epileptic and normal cortex, and continuous electrical stimulation evoked large increases in (3H)GABA release in both preparations. Preseizure efflux of (3H)GABA was the same in the two preparations in all experiments. Results do not support the hypothesis that seizure susceptibility of chronically denervated cortex is due to the interruption of recurrent inhibitory pathways. 22 references. (Author abstract modified)

0004084 Reigle, Thomas G.; Huff, Joseph W. Dept. of Pharmacology, School of Pharmacy, University of Georgia, Athens, GA 30602 **Single-dose tolerance to the effects of morphine on brain 3-methoxy-4-hydroxyphenylethylene glycol sulfate.** Biochemical Pharmacology. 29(16):2249-2251, 1980.

The relationships betweeen increased brain norepinephrine turnover, opiate action, and tolerance development were characterized by evaluating the ability of morphine to induce single dose tolerance to its effect on brain 3-methoxy-4-hydroxyhenylethylene glycol sulfate (MOPEG-SO4), and the ability of cycloheximide, an inhibitor of protein synthesis, to antagonize the development of single dose tolerance to this effect was assessed. Results illustrate the development of single dose tolerance to the effect of morphine on brain MOPEG-SO4 and the prevention of this tolerance by prior administration of sufficient doses of cycloheximide. These findings are comparable to those obtained from evaluations of the analgesic, and other, actions of morphine and, together with previous evidence, greatly strengthen the concept that the production of an increase in brain norepinephrine turnover is a specific component of the pharmacological actions of narcotic analgesics. 14 references.

0004085 Reigle, Thomas G.; Orsulak, Paul J.; Avni, Jacov; Platz, Patricia A.; Schildkraut, Joseph J. Neuropsychopharmacology Lab., Massachusetts Mental Health Center, Dept. of Psychiatry, Harvard Medical School, Boston, MA 02115 **The effects of tranylcypromine isomers on norepinephrine-H3 metabolism in rat brain.** Psychopharmacology. 69(2):193-199, 1980.

The effects of d-tranylcypromine and l-tranylcypromine on the disposition and metabolism of intracisternally administered l-norepinephrine-H3 were studied in rat brain. Both isomers inhibited the deamination of norepinephrine-H3. However, d-tryanylcypromine was considerably more potent than the l-isomer in this respect. In addition, the l-isomer of tranylcypromine was found to enhance the disappearance of endogenous and tritiated norepinephrine from brain. Although this action appeared to result from an increase in catecholamine release, the possibility of uptake inhibition could not be eliminated. The l-isomer of tranylcypromine enhanced the disappearance of norepinephrine-H3 from brain when administered both 20 and 90 min following intracisternal injection of the label. Comparable doses of d-tranylcypromine did not exhibit this effect. Larger increases in brain levels of normetanephrine-H3 were produced by d,l-tranylcypromine than by either the d-isomer or the l-isomer alone, indicating that the racemic mixture may produce the greatest increase in the interaction of norepinephrine with its postsynaptic receptors. 26 references. (Author abstract modified)

0004086 Retz, Konrad Charles. University of Iowa **Mechanisms of opiate tolerance and dependence in the central nervous system: investigation of the rates. (Ph.D. dissertation).** Dissertation Abstracts International. 40(5):2135-B, 1979. Ann Arbor, Univ. Microfilms No. 7924521, 154p., 1979.

The postulate of the enzyme expansion hypothesis that macromolecular synthesis is required for the development of opiate tolerance and dependence was tested by using morphine in rats.

Following the acute administration of morphine to rats the rates of synthesis of secretory membrane and nonsecretory proteins were reduced by 80% in the liver, whereas the rates in whole brain were unaffected. The site of inhibition of protein synthesis was determined to be at the level of polypeptide elongation as inferred from analysis of the size and content of polysomes and the flow of 3H-leucine from the nascent polypeptides to released proteins. Morphine-induced respiratory depression, hypoxia, and inhibition of oxidative phosphorylation were found to lead to inhibition of ATP synthesis and the utilization of ATP for biosynthetic processes including protein synthesis eventually depletes cellular energy reserves to levels insufficient for protein synthesis. When rats were made dependent on morphine the rates of synthesis of secretory/membrane proteins in the bound polysome compartment of the striatum septum and pons medulla were enhanced as much as 20 to 28%. Results suggest that the enhanced synthesis of secretory/membranes in specific brainstem regions is necessary for the development of tolerance to and physical dependence on opiates, thereby providing support for the role of macromolecular synthesis. (Journal abstract modified)

0004087 Revuelta, A. V.; Cheney, D. L.; Costa, E.; Lander, N.; Mechoulam, R. Costa: Lab. of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Reduction of hippocampal acetylcholine turnover in rats treated with (-)-delta8-tetrahydrocannabinol and its 1',2'-dimethyl-heptyl homolog.** Brain Research. 195((2):445-452, 1980

The effects of (-)-delta8-tetrahydrocannabinol (THC), ()-delta 8-THC, and the dimethyl-heptyl (DMH) homolog of (-)-delta8-THC (delta8-THC-DMH) were compared with the action of (-)-delta9-THC on the turnover rate of acetylcholine in various brain areas. The data demonstrate that (-)-delta8-THC-DMH, (-)-delta9-THC, and (-)-delta8-THC all specifically reduce the turnover rate of acethylcholine in the hippocampus in a dose dependent manner ((-)-delta8-THC-DMH greater than (-)-delta9-THC greater than (-)-delta8-THC) without altering the acetylcholine or choline content (except for high doses of (-)-delta8-THC-DMH). The ()-isomer of delta8-THC failed to change any cholinergic parameter. The selectivity of action suggests that the tetrahydrocannabinoids may activate specific transmitter receptors which indirectly modulate the activity of the cholinergic neurons in the septal/hippocampal pathway. 39 references (Author abstract)

0004088 Ricaurte, George A.; Schuster, Charles R.; Seiden, Lewis S. Seiden: Dept. of Pharmacological and Physiological Sciences, University of Chicago, Chicago, IL 60637 **Long-term effects of repeated methylamphetamine administration on dopamine and serotonin neurons in the rat brain: a regional study.** Brain Research. 193(1):153-163, 1980.

Repeated high doses (25 and 100mg/kg) of methylamphetamine produced long-term depletions of dopamine (DA) and serotonin (5-HT) in the male Sprague-Dawley rat brain. DA depletions were most pronounced in the neostriatum and substrantia nigra; 5-HT levels were most reduced in the amygdala, frontal cortex, and neostriatum. The hypothalamus was relatively resistant to the effects of methylamphetamine on DA and 5-HT. Serotonergic systems appeared to be more sensitive than DA systems to the neurotoxic actions of methylamphetamine. 35 references. (Author abstract modified)

0004089 Robinson, J. H.; Deadwyler, S. A. Dept. of Physiology and Pharmacology, Bowman Gray School of Medicine, 300 S. Hawthorne Ave., Winston-Salem, NC 27103 **Morphine excitation: effects on field potentials recorded in the in vitro hippocampal slice.** Neuropharmacology. 19(6):507-514, 1980.

The hippocampal slice preparation was used to study the effects of morphine on CA1 field potentials recorded in vitro. Morphine sulfate produced two distinct excitatory effects when added to the bathing media or applied directly to the slice via a pressure pipette injection system. First, morphine produced an increase in amplitude and a reduction in latency of the CA1 population spike elicited by orthodromic stimulation of stratum radiatum, without any change in the amplitude of the synaptic field potential. This was accompanied by a pronounced shift to the left of the population spike input/output curve indicating an increase in excitability of the CA1 neurons. At higher stimulus intensities, orthodromic stimulation produced a series of multiple peaks following the original population spike where only a single spike had been present before morphine application. The increase in population spike amplitude was partially reversed by application of the morphone antagonist naloxone, but naloxone did not affect the number of peaks elicited in morphine treated slices. Pentobarbital was effective in reducing the number of stimulus elicited peaks but did not reduce the increase in the population spike. The possibility that these effects are mediated by morphine-induced inhibition of GABAergic synapses in the hippocampus is discussed. 40 references. (Author abstract)

0004090 Rogawski, Michael A.; Aghajanian, George K. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Norepinephrine and serotonin: opposite effects on the activity of lateral geniculate neurons evoked by optic pathway stimulation.** Experimental Neurology. 69(3):678-694, 1980.

The effects of norepinephrine (NE) and serotonin (5-HT) on the activity of lateral geniculate nucleus (LGN) single units driven by electrical stimulation of the afferent visual pathway at the level of the optic chiasm were investigated. NE caused caused a marked facilitation of both the short latency (2 to 4 ms) and the delayed (70 to 230 ms) responses to such stimulation. The alpha-adrenoceptor antagonist phentolamine, which by itself had no consistent effect on evoked activity, strongly diminished the response to NE. In contrast to NE, 5-HT was a powerful depressant of electrically evoked activity; neither phentolamine nor the 5-HT antagonist methysergide antagonized this response. Firing of LGN units evoked by flashes of light was also facilitated by NE and depressed by 5-HT. It is concluded that LGN relay neurons exhibit the following unique features in their responsiveness to monoamines: 1) microiontophoretically applied NE facilitates, but 5-HT depresses, the spontaneous or synaptically evoked activity of virtually every cell; and 2) there is no dissociation between the actions of NE on spontaneous and evoked activity, as is the case in other brain regions. 55 references. (Authjor abstract modified)

0004091 Rosenberg, Jack Manny. St. John's University **The effects of neurolepties and vitamin-B6 on serum prolactin levels in the male rat. (Ph.D. dissertation).** Dissertation Abstracts International. 40(3):1144-B, 1979. Ann Arbor, Univ. Microfilms No. 7920961, 117p., 1979.

The prolactin stimulating properties of chlorpromazine hydrochloride, fluphenazine hydrochloride, perphenazine, prochlorperazine edisylate, and trifluoperazine hydrochloride (phenothiazines); haloperidol (a butyrophenone) chlorprothixene (a thioxanthene); loxapone succinate; and molindone hydrochloride were compared on the rat. A close correlation between the prolactin stimulating potency of each drug in rats and their clinically defined therapeutic potency is reported. Whether vitamin B6 inhibits prolactin release was also studied. Pyridoxine hydrochloride suppressed chlorpromazine-induced prolactin rise; but the suppression was significantly less than that produced by bromocriptine; and pyridoxal hydrochloride failed to suppress prolactin. It is concluded that some support is demonstrated for the

theory that pyridoxine hydrochloride partially inhibits prolactin by a mechanism not involving dopamine. (Journal abstract modified)

0004092 Rosenblatt, Jack E.; Del Carmen, Rebecca; Wyatt, Richard Jed. Lab. of Clinical Psychopharmacology, Div. of Special Mental Health Research, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **A high affinity GTP binding site in rat brain.** European Journal of Pharmacology. 64(4):365-366, 1980.

The presence of specific high affinity site binding sites for tritiated guanosine triphosphate (GTP) male Sprague-Dawley rat caudate was demonstrated. Scatchard analysis of GTP displaceable 3H-GTP binding revealed two populations of binding sites, one with high affinity and low capacity and the other with low affinity and high capacity. Specific binding of 3H-GTP was not displaced by adenosine triphosphate, guanine, guanosine, dopamine, or haloperidol. Specific binding of 3H-GTP was also observed in cerebral cortex, hippocampus, cerebellum, hypothalamus, and medulla/pons. 2 references.

0004093 Ross, Svante B.; Kelder, Diana. Research and Development Laboratories, Astra Lakemedel AB, S-151 85 Sodertalje, Sweden **Inhibition of 3H-dopamine accumulation in reserpinized and normal rat striatum.** Acta Pharmacologica et Toxicologica. 44(5):329-335, 1979.

The inhibitory potencies of 27 compounds on the accumulation of tritiated dopamine (DA) in synaptosome rich striatal homogenates from normal and reserpinized male Sprague-Dawley rats were determined. Amphetamine-like stimulants (phenmetrazine, phenethylamine derivatives, and tryptamine derivatives) were considerably more potent in the reserpinized preparation than in the normal one. Methylphenidate-like compounds (amfonelic acid, mazindol, benztropine, pipradrol, nomifensine, and cocaine) had similar potencies in the two preparations. It is suggested that the compounds enhanced by reserpine are more potent as DA releasing agents than as inhibitors of DA uptake, whereas compounds in second group are more potent as uptake inhibitors. 24 references. (Author abstract modified)

0004094 Roth, Bryan L.; Galloway, Matthew P.; Coscia, Carmine J. Coscia: E. A. Doisy Dept. of Biochemistry, St. Louis University School of Medicine, St. Louis, MO 63104 **The effects of morphine on catecholamine metabolism during postnatal development.** Brain Research. 197(2):561-564, 1980.

The effects of morphine on catecholamine metabolism during postnatal development were investigated in rats. At various days after birth, rat pups were given intraperitoneal injections of test substances and sacrificed 1.5 h later. Although data obtained with mature rats argues that opiate-induced elevations in striatal dihydroxyphenylacetic acid (DOPAC) levels are mediated through a presynaptic opiate receptor, the capability for eliciting this response may not appear until about 6 days after birth. Furthermore, the effect becomes optimal at about 15 days postnatally. This contrasts with the demonstration of stereospecific opiate receptors at birth in the striatum, and may reflect the rapid rise in immunoreactive enkephalin between birth and about postnatal day 6. Since there was a response to morphine in the adrenal medulla on postnatal day 3, it appears that the system mediating this reflex matures somewhat earlier than does that in the striatum. 17 references.

0004095 Ruegg, Urs T.; Hiller, Jacob M.; Simon, Eric J. Simon: Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Solubilization of an active opiate receptor from Bufo marinus.** European Journal of Pharmacology. 64(4):367-368, 1980.

An active stereospecific opiate binding site was solubilized from toad (Bufo marinus) brain membranes. Digitonin (1%) extracted 30 to 40% of opiate binding along with 20 to 30% of the membrane protein into the solubilized fraction. Bound 3H-diprenorphine was displaced by naloxone or levorphanol but not by dextrophan, indicating that stereospecificity was maintained. 5 references.

0004096 Sahley, Tony L.; Berntson, Gary G. Berntson: 202 OSU Research Center, 1314 Kinnear Road, Columbus, OH 43212 **Antinociceptive effects of central and systemic administration of nicotine in the rat.** Psychopharmacology. 65(3):279-283, 1979.

The antinociceptive properties of nicotine were examined in the rat in order to clarify the receptor basis of such potential antinociceptive actions. Nicotine was found to exert a potent antinociceptive action on thermal stimuli. This action could be blocked by centrally active nicotinic or muscarinic blockers implicating both classes of cholinergic receptors. Results suggest a central site of action for the antinociceptive action of nicotine. Results also support the suggestion that nicotine may selectively reduce sensitivity to certain classes of pain stimuli, perhaps through a central releasing action on acetylcholine. 24 references. (Author abstract modified)

0004097 Scherman, Daniel; Henry, Jean-Pierre. Service de Biochimi-Physique, Institut de Biologie Physico-Chimique, Paris, France **Effect of drugs on the ATP-induced and pH-gradient-driven monoamine transport by bovine chromaffin granules.** Biochemical Pharamacology. 29(13):1883-1890, 1980.

The effect of drugs on the ATP-induced and pH gradient driven monoamine transport by bovine chromaffin granules was investigated. Rerserpine, tetrabenzine, and the neuroleptics chlorpromazine and haloperidol blocked the ATP dependent uptake of noradrenaline and tyramine by ghosts derived from bovine chromaffin granules. The drugs did not affect chromaffin granules energization since they were without any effect on the membrane ATPase activity and on the transmembrane potential and pH gradient generated by the ATP dependent H translocase. Differences were observed in the inhibitory effect of the drugs on the monamine uptake by ghosts acidic with respect to the external medium. These differences were accounted for by the existence under these conditions of two mechanisms of uptake, as shown by kinetic experiments. Noradrenaline was taken up by a carrier mediated process which was blocked by all drugs, whereas tyramine transport involved nonspecific diffusion of its unprotonated form, a process which is sensitive to neuroleptics and high doses of rerserpine. From the kinetic and oharmacological studies of tyramine uptake, it is concluded that the ATP dpeendent active transport of monoamines requires a carrier mediated process even for amines which are rapidly transported by nonspecific diffusion through the membrane. 30 references. (Author abstract modified)

0004098 Schlemmer, R. Francis, Jr.; Casper, Regina C.; Narasimhachari, Nedathur; Davis, John M. Research Dept., Illinois State Psychiatric Institute, Chicago, IL 60612 **Clonidine-induced hyperphagia and weight gain in monkeys.** Psychopharmacology. 61(2):233-234, 1979.

The effect of the alpha-noradrenergic receptor agonist, clonidine, on food intake and weight was examined in 10 adult stumptail macaque monkeys. An intramuscular injection of 0.1mg/kg of clonidine HCL for 7 consecutive days significantly increased food intake from baseline levels throughout treatment. All but two monkeys gained weight during clonidine treatment, with seven animals gaining from 5% to 15% of their original bodyweihtg by the end of 1 week. The possible utility of cloni-

dine in the treatment of eating disorders in humans, such as anorexia nervosa, is noted. 9 references. (author abstract modified).

0004099 Schmeling, W. T.; Hosko, M. J. Medical College of Wisconsin, Dept. of Pharmacology, P.O. Box 26509, Milwaukee, WI 53226 **Hypothermic effects of intraventricular and intravenous administration of cannabinoids in intact and brainstem transected cats.** Neuropharmacology. 19(6):567-573, 1980.

Delta 9-tetrahydrocannabinol (THC) and the synthetic cannabinoid Dimethylheptylpuran (DMHP) were injected into ventricle III or IV of chronically implanted unanesthetized cats to determine the effect on body temperature. The hypothermia induced by administration of THC into ventricle IV was faster in onset and reached a greater maximum than that induced by ventricle III administration. Five hundred micrograms of THC produced significantly less hypothermia than interventricular microinjection. Administration of THC to animals with a midcollicular transection produced significant decreases in blood pressure, heartrate, and body temperature when compared to animals receiving vehicle alone. Cats transected at C-1 were utilized to determine the rate at which body temperature was lost in animals unable to temperature regulate. THC had no effect in these preparations indicating that direct peripheral mechanisms have little or no role in THC-induced hypothermia. It is further noted that THC had little effect on blood pressure or heartrate in C-1 transected animals. These findings suggest a caudal brainstem site of action for the hypothermic effect of the cannabinoids. 44 references. (Author abstract modified)

0004100 Schmidt, Richard Hall. University of Iowa **Regenerative growth of central noradrenergic neurons in the developing rat brain after lesions with 6-hydroxydopamine: a model of noradrenergic neuronal development. (Ph.D. dissertation).** Dissertation Abstracts International. 40(5):2149-B, 1979. Ann Arbor, Univ. Microfilms No. 7924525, 277p., 1979.

The interaction of 6-hydroxydopamine (6OHDA) with the postnatal development of the noradrenergic system was studied in the rat to elucidate the mechanisms participating in the control of developmental and regenerative growth. It was determined that the initial consequence of such treatment was an equivalent loss of norepinephrine (NE), dopamine beta-hydroxylase (DBH), and tyrosine hydroxylase from both the cerebral cortex and the cerebellum. With the use of lesions in the locus coeruleus indications were found that the recovery of cerebellar noradrenergic innervation after 6OHDA was due to regenerative growth from the locus coeruleus, but with a resultant increase in the number of terminals; the larger elevations in NE and DBH resulted from synaptic vesicle shunting from the degenerated forebrain projection, and that a significant fraction of the ipsilateral cerebral cortical and cerebellar noradrenergic innervation is derived as collaterals from the same neurons. Dose response studies with intracisternally administered 6OHDA were also performed. The regenerative potential of the cerebellar projection was found to be maximal closet to birth and to subside gradually but fully by the end of the first postnatal week. (Journal abstract modified)

0004101 Share, N. N. Dept. of Pharmacology, Merck Frosst Laboratories, Kirkland, Quebec, Canada H9R 4P8 **Cyclobenzaprine: studies on its site of muscle relaxant action in the cat.** Neuropharmacology. 19(8):757-764, 1980.

The tonic vibration reflex (TVR) induced by vibration of the gastrocnemius-soleus (GS) muscle was reduced by cyclobenzaprine in decerebrate cats but not in high spinal preparations. Cyclobenzaprine reduced or abolished GS muscle contractions elicited through direct activation of brainstem regions as well as TVR responses facilitated by brainstem stimulation. Direct activation of spinal regions and TVRs facilitated by spinal stimulation were only moderately sensitive to cyclobenzaprine. Results indicate that cyclobenzaprine acts on motor systems originating in the brainstem to exert its muscle relaxant effects. 20 references. (Author abstract modified)

0004102 Siegel, Karen M. Hall. Fordham University **Catecholamine synthesis in brain: effect of mudcimol on norepinephrine synthesis in hypothalamus. (Ph.D. dissertation).** Dissertation Abstracts International. 40(3):1167-B, 1979. Ann Arbor, Univ. Microfilms No. 7918301, 155p., 1979.

Muscinol was used in vivo to determine whether it can alter catecholamine synthesis in rat brain. Synaptosomal preparations from caudate nucleus and from brainstem were prepared from rats injected with muscimol, but neither tissue evidenced a response to the drug; when hypothalamic tissue was used, however, there was an effect on the synthesis of catecholaimes from labeled tyrosine. An assay of dopamine-beta-hydroxylase indicated that muscimol causes an increase in its activity consistent with the increase in synthesis of norepinephrine (NE) at the same dose. Bicuculline, a GABA-receptor blocker, antagonized the muscimaol effect in hypothalamus indicating that muscimol acts on postsynaptic GABA receptor sites. It is surmised that muscimol affects a brainstem area containing noradrenergic cell bodies, and that this action is communicated to the hypothalamus via noradrenergic projections, where itis experessed in the observed increase in the rate of synthesis of NE. (Journal abstract modified)

0004103 Simmonds, M. A. Dept. of Pharmacology, School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX, England **A site for the potentiation of GABA-mediated responses by benzodiazepines.** Nature. 284(No. 5756):558-560, 1980.

To investigate the possible association between benzodiazepine binding sites in the neuronal membrane and GABA receptors, quantitative studies were made in vitro on neuronal depolarizations mediated by GABA receptor activation. Flurazepam was shown to attenuate preferentially the action of picrotoxin rather than bicuculline, and a model is suggested for the site of action of these drugs within the GABA response mechanism. The model suggests that either: 1) flurazepam increases the duration of ion channel opening for each GABA receptor activation, or 2) only a proportion of the GABA receptor activations results in channel opening and flurazepam increases that proportion. It also seems that there is no requirement for a fixed ratio of benzodiazepine sites to GABA receptors in the neuronal membrane. While it is clear that responses to GABA receptor activation can be modulated at a number of different sites. 20 references.

0004104 Simon, Eric J.; Bonnet, Kenneth A.; Hiller, Jacob M.; Rieman, Mark W.; Merrifield, R. B. Dept. of Medicine, New York University Medical Center, New York, NY 10016 **Opioid activity of synthetic and naturally occurring enkephalin peptides.** Biochemical Pharmacology. 28(22):3333-3337, 1979.

Analogs of methionine-enkephalin with alterations at the N-terminus or C-terminus were tested for opiate receptor affinity, stability in brain homogenates, and in vivo analgesic potency in male Sprague-Dawley rats. Alterations at the N-terminus increased the stability of peptides incubated in brain homogenates. Intracerebral injection of an analog with D-alanine added at the C-terminus resulted in potent analgesia, with a longer duration of action than methionine-enkephalin. Results suggest that peptidase hydrolysis at the N-terminus may not be the only important mechanism of opioid peptide inactivation. 25 references. (Author abstract modified)

0004105 Singh, Pritam; Dufour, Maurice; D'Auteuil, Claire. Dept. de Pharmacologie, Faculte de Medecine, Universite Laval, Quebec G1K 7P4, P. Q. Canada **Influence of drug associations incorporating psychotropic drugs and theophylline on cerebral cyclic AMP in mice.** Progress in Neuro-Psychopharmacology. 4(1):91-100, 1980.

The effects of combinations of psychotropic drugs and theophylline on cerebral cyclic AMP were investigated. Administration of chlorpromazine was found to significantly decrease whole brain cyclic AMP; the decreases induced by phenobarbital, promazine, and theophylline were not significant. The association of theophylline eith promazine significnatly increased whole brain cyclic AMP. Theophylline counteracted the diazepam-induced decrease in plasma cyclic AMP. A marked decrease in cortical cyclic AMP induced by theophylline, chlorpromazine, promazine, and phenobarbital was noted. This decrease was prolonged and was evident even after 1 hour. Although theophylline, chlorpromazine, promazine, and phenobarbital did not affect cyclic AMP content of striatum, the association of theophylline with chlorpromazine or promazine resulted in significant lowering of striatal cyclic AMP. 21 references. (Author abstract modified)

0004106 Sitkiewicz, D.; Skonieczna, M.; Krzywicka, K.; Dziedzic, E.; Staniszewska, K.; Bicz, W. Dept. of Drug Metabolism, Institute of Biopharmacy, AM, ul. Banacha, 02-097 Warsaw, Poland **Effect of organophosphorus insecticides on oxidative processes in rat brain synaptosomes.** Activitas Nervosa Superior. 21(4):276-277, 1979.

The effect of organophosphorus insecticides on oxidative processes in rat brain synaptosomes was investigated. The influence of dipterex, DDVP, Ronnel, and its oxygen analogue (OAR) on AChE activity was tested on nonsolubilized fractions in two types of experiments at low or high ionic strength of the buffers. Results demonstrate that DDVP, a stronger inhibitor of AChE, did not change the rate of respiration as well as the process of oxidative phosphorylation in synaptosomes. It is assumed that the inhibition of AChE associated with synaptosomal membranes does not affect the mitochondrial oxidations. The lack of correlation between AChE inhibition produced by OAR, and the ability of the latter to affect the process of ATP formation, also confirm this supposition. 4 references.

0004107 Skonieczna, M.; Sitkiewicz, D.; Orlowska, E.; Bicz, W. Dept. of Drug Metabolism, Institute of Biopharmacy, AM, ul. Banacha, 02-097 Warsaw, Poland **Effect of Chlorfenvinphos and its chemical analogues on the oxidative phosphorylation in rat brain and liver mitochondria.** Activitas Nervosa Superior. 21(4):274-275, 1979.

The effect of Chlorfenvinphos and its chemical analogues on the oxidative phosphorylation in rat brain and liver mitochondria were examined. Mitochondria were isolated by the differential centrifugation method, and oxygen consumption with succinate as substrate and oxidative phosphorylation were measured polarographically with Clark type oxygen electrodes. The data are not compatible with the hypothesis that insecticides which contain chlorinated aromatic ring can alter the process of ATP formation, but in two different ways: uncoupling of oxidative phophorylation or inhibition of oxidative phosphorylation. 6 references.

0004108 Smith, James E.; Co, Conchita; Freeman, Mark E.; Sands, Michael P.; Lane, John D. Psychiatry Research Unit, Dept. of Psychiatry, Louisiana State University Medical Center, Shreveport, LA 71130 **Neurotransmitter turnover in rat striatum is correlated with morphine self-administration.** Nature. 287(5778):152-154, 1980.

The striatal turnover rates of dopamine (DA), noradrenaline (NA), aspartate (Asp), glutamate (Glu), GABA, and glycine (Gly) were determined in rats self-administering morphine and in yoked morphine infused and yoked vehicle infused littermates to elucidate the neurochemical effects of the drug alone and the effects of the drug self-administration milieu. The striatal content of the putative neurotransmitters and amino acids did not differ in any of the treatment conditions, whereas turnover rates were very different in the yoked morphine infused and self-administering animals. Passive morphine infusions alone resulted in an increase in the turnover rates of DA, Glu, Gly, and a decrease in NA utilization. Turnover rates of DA, NA, Asp, Glu, and GABA were almost twice and Gly almost half as high in the self-administering rats as in the yoked morphine infused animals. These data indicate that striatal catecholaminergic systems are important in mediating opiate reinforcement, and that neurotransmitter systems are directly involved in morphine reward. 24 references.

0004109 Smith, Susan Harvell. Virginia Commonwealth University/Medical College of Virginia **Immunosuppressant activity of naturally occurring and synthetic cannabinoids. (Ph.D. dissertation).** Dissertation Abstracts International. 40(5):2150-B, 1979. Ann Arbor, Univ. Microfilms No. 7922648, 201p., 1979.

Whether a structural modification of delta-9-tetrahydrocannabinol (delta-9-THC) would result in a more potent immunosuppressant agent devoid of CNS activity was studied. Humoral immunity to a T-dependent antigen was measured in mice given cannabinoids 2 days after immunization with sheep red blood cells. Delta-9-THC reduced spleen IgM hemolytic plaque forming cells. Delta-8-THC, 1-methyl delta-8-THC, and abnormal delta-8-THC were more potent. This immunosuppression was not related to CNS activity. All four cannabinoids suppressed the delayed typed hypersensitivity (DTH) response 35 to 64% while 1-methyl delta-8-THC suppressed the DTH response 88%. Results of experiments using local adoptive transfer of the DTH response suggest that 1-methyl delta-8-THC reduced the DTH response by acting on accessory cells or other factors necessary for the DTH footpad swelling response. (Journal abstract modified)

0004110 Snyder, E. W.; Shearer, D. E.; Dustman, R. E.; Beck, E. C. Veterans Administration Medical Center, Salt Lake City, UT 84148 **Methadone-induced changes in the visual evoked response recorded from multiple sites in the cat brain.** Psychopharmacology. 63(1):89-95, 1979.

Visual evoked responses (VERs) and EEGs were recorded following the i.p. administration of five doses of methadone to 12 adult cats which were implanted with cortical and subcortical electrodes. Additional cats, subjected to the same drug regimen, were used to evaluate plasma methadone concentrations. Doses of methadone that produced plasma concentrations between 80 and 190ng/ml differentially affected VERs recorded from cortical and subcortical sites. Behavioral changes were clearly evidenced in some cats at lower doses of methadone. Therefore, the data suggest that those structures evaluated electrophysiologically did not reflect the full force of the drug's action as evidenced by its effect on behavior, that cortical and subcortical recording sites have differential sensitivities, and that one clearly defined, principal site of action of methadone is absent in the cat. 44 references. (Author abstract modified)

0004111 Sosinski, Eugeniusz. Zaklad Neurolpatologii AM, ul. Przybyszewskiego 49, 60-355 Poznan, Poland /Neuropathological changes in the rat brain following intoxication with Ceresan./ **Zmiany neuropatologiczne w mozgu szczura w nastepstwie zatrucia Ceresanem.** Neuropatologia Polska. 17(4):585-593, 1979.

The effect of methoxyethylmercury chloride (Ceresan) on brain morphology was studied. Wistar rats of both sexes were given Ceresan intragastrically in 200mg, 100mg, and 50mg doses. Lesions of different intensity and character (from ischemic changes to liquefaction) involved neurocytes of all the brain structures. Edematous changes were observed in the white matter, being most intensive within the brainstem and glial cells. Activation and focal proliferation of ependymal cells and subependymal glia became apparent in all structures of the central nervous system. The microscopic picture showed no variations related to the dose or administration period. Pathogenic implications of the observed changes are discussed. 13 references. (Journal abstract)

0004112 Sowers, J. R.; Sollars, E.; Barrett, J. D.; Sambhi, M. P. Endocrine and Hypertension Laboratories, V.A. Medical Center, Sepulveda, CA 91343 **Effect of L-dopa and bilateral nephrectomy on the aldosterone response to metoclopramide.** Life Sciences. 27(6):497-501, 1980.

To investigate the mechanism of action of metoclopramide (MCP) in increasing plasma aldosterone (PA), rats were studied after pretreatment of L-dihydroxyphenylalanine (L-dopa) and after bilateral nephrectomy. Intraarterial MCP resulted in a significant elevation in PA and prolactin (PRL) at 5 min and plasma renin activity (PRA) at 10 min without altering serum potassium levels. Preadministration of L-dopa delayed and markedly blunted PA, PRL, and PRA responses to MCP. In seven rats, studied 30 hours after bilateral nephrectomy, the PRA was measurable, but displayed no response to MCP. In contrast, the PA and PRL responses to MCP were not significantly affected. L-dopa-induced suppression of PRA and PA was prevented by preadministration of MCP. These results suggest that dopaminergic modulation of PA secretion occurs independently of the renin/angiotensin system. 16 references. (Author abstract modified)

0004113 Squibb, R. E.; Carmichael, N. G.; Tilson, H. A. National Institute of Environmental Health Sciences, P. O. Box 12233, Research Triangle Park, NC 27709 **Behavioral and neuromorphological effects of triethyl tin bromide in adult rats.** Toxicology and Applied Pharmacology. 55(1):188-197, 1980.

The repeated administration of triethyl tin bromide (TET) to male rats was found to produce dose and time dependent reductions in body weights and food and water consumption. Tests showed decreases in forelimb and hindlimb grip strength and startle responsiveness. Histologic examination immediately after the 2 week dosing period showed that in all dose groups there was intramyelinic edema of major CNS white matter tracts, the severity of which varied according to the dose. Four weeks after cessation of TET dosing, body weights of the treatment groups had almost recovered to control group values. There was complete recovery of food and water consumption. Retests for functional performance indicate complete recovery of all measures with the exception of continued reduction of startle responsiveness to an air puff stimulus. Histologic examination after the 4 week recovery period indicated that the 1.0mg/kg dose groups was indistinguishable from controls, while all of the 2.0mg/kg dose group samples were still moderately edematous. These results demonstrate that specific behavioral tests can show toxic effects of TET in otherwise asymptomatic animals. 16 references. (Author abstract modified)

0004114 Steger, R. W.; Sonntag, W. E.; Van Vugt, D. A.; Forman, L. J.; Meites, J. Meites: Dept. of Physiology, Michigan State University, East Lansing, MI 48824 **Reduced ability of naloxone to stimulate LH and testosterone release in aging male rats; possible relation to increase in hypothalamic met5-enkephalin.** Life Sciences. 27(9):747-753, 1980.

The reduced ability of naloxone to stimulate luteinizing hormone (LH) and testosterone release in aging male rats was investigated and its possible relation to increases in hypothalamic met5-enkephalin was examined. The specific opiate antagonist, naloxone, previously shown to increase serum LH in mature male rats, exhibited relatively little ability to raise serum LH and testosterone levels in old (18 to 20 months) as compared to young (4 to 5 months) male rats. The brain opiate, met5-enkephalin, which depresses LH, was found to be significantly higher in the hypothalamus of old than of young male rats. These observations suggest that hypothalamic opiates may be partially responsible for the lower serum LH and testosterone levels in old male rats, and for reduced release of these hormones in response to naloxone administration. 18 references. (Author abstract modified)

0004115 Stine, S. M.; Yang, H.-Y. T.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Release of enkephalin-like immunoreactive material from isolated bovine chromaffin cells.** Neuropharmacology. 19(7):683-685, 1980.

The enkephalin-like immunoreactive material stored in primary cultures of bovine chromaffin cells was released spontaneously when these cells were transferred from the culture medium to Krebs-Ringer buffer. Potassium (56mM) and acetylcholine (ACh, 0.0001M) increased the rate of spontaneous release in a calcium dependent fashion. Preliminary studies suggest that nicotinic receptors are involved in mediating the release of enkephalin-like peptides elicited by ACh. 10 references. (Author abstract modified)

0004116 Stoof, Johannes C.; Horn, Alan S.; Mulder, Arie H. Dept. of Neurology, Free University Medical Faculty, van der Boechorststraat 7, 1081 BT Amsterdam,The Netherlands **Simultaneous demonstration of the activation of presynaptic dopamine autoreceptors and postsynaptic dopamine receptors in vitro by N,N-dipropyl-5,6-ADTN.** Brain Research. 196(1):276-281, 1980.

The simultaneous demonstration of the activation of presynaptic dopamine autoreceptors and postsynaptic dopamine (DA) receptors in vitro by N,N-dipropyl-5,6-ADTN, a derivative of 2-amino-5,6-dihydroxytetrahydronaphthalene, a DA analogue with a semirigid molecular conformation, is reported. This demonstration was achieved by labeling slices with both (3H)DA and (l4C)choline and utilizing a depolarizing stimulus of moderate intensity to induce transmitter release. The inhibitory effect of N,N-dipropyl-5,6-ADTN on the K-induced release of both radiolabelled DA and ACh were antagonized by fluphenazine, indicating that N,N-dipropyl-5,6-ADTN not only stimulates postsynaptic DA receptors, mediating the modulation of ACh release, but also activates DA autoreceptors, which directly modulate DA release. 22 references.

0004117 Suga, Masakazu. Dept. of Neurology, Brain Research Institute, Niigata University, Asahimachi, Niigata 951, Japan **Effect of long-term L-Dopa administration on the dopaminergic and cholinergic (muscarinic) receptors of striatum in 6-hydroxydopamine lesioned rats.** Life Sciences. 27(10):877-882, 1980.

Tritiated spiperone and quinuclidinyl benzilate (QNB) binding were measured in the striatum of male Wistar rats given unilateral 6-hydroxydopamine lesions and treated with L-dopa (200mg/kg/day) for 30 days. Binding of 3H-spiperone increased 73% and binding of 3H-QNB decreased 14% in the lesioned striata, prior to L-dopa treatment. Tritiated spiperone binding in the lesioned side was 21% lower in animals given L-dopa than in those not given L-dopa; in animals treated with L-dopa, 3H-spiperone binding was 27% higher in the lesioned side than in the intact side. The binding of 3H-QNB did not differ signifi-

cantly in the lesioned and intact sides of animals treated with L-dopa. 30 references. (Author abstract modified)

0004118 Sun, C. L.; Kopin, I. J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Plasma catecholamines and direct stimulation of rat hypothalamus.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1422-1424).

The effects of direct electrical stimulation of various areas of the male Sprague-Dawley rat hypothalamus on blood pressure (BP), heartrate (HR), and plasma catecholamines were examined. Low intensity stimulation of the anterior area (AH) evoked a slight depressor response with increased HR and plasma epinephrine (EPI). Higher intensity stimulation of AH or low intensity stimulation of the posterior area (PH) resulted in a pressor response and increased plasma EPI. Norepinephrine levels were not greatly increased even when BP was markedly increased. Stimulation of lateral or medial areas evoked only small responses. The responses evoked by stimulation of the PH were markedly attenuated by chlorisondamine, clonidine, or alpha-methyldopa. The effects of atropine, methylatropine, phentolamine, propranolol, diazepam, and haloperidol are also reported, and the involvement of alpha-adrenergic and GABA synapses in mediating changes in autonomic outflow is discussed. 3 references. (Author abstract modified)

0004119 Suva, J.; Janousek, I.; Svejnohova, D. Karlovarska 48, 301 67 Plzen, Czechoslovakia **Early lithium levels in rat serum, blood cells and some organs.** Activitas Nervosa Superior. 22(2):121-122, 1980.

Early lithium levels in rat serum blood cells and organs were assessed following a single dose of 0.5 mM LiCl solution (1mmol/kg). One hour postinjection, animals were decapitated and lithium was assayed by atomic absorption spectrometry. Lithium appeared in the biological fluids and organs soon after being resorbed from the subcutaneous tissue. The maximum tissue level was found in the kidneys, followed by the liver, the erythrocytes, and brain. 1 reference.

0004120 Suzuki, Osamu; Hattori, Hideki; Asano, Minoru; Oya, Masakazu; Katsumata, Yoshinao. Dept. of Legal Medicine, Hamamatsu University School of Medicine, Hamamatsu 431-31, Japan **Inhibition of monoamine oxidase by d-methamphetamine.** Biochemical Pharmacology. 29(14):2071-2073, 1980.

The inhibition of type-A and type-B monoamine oxidase (MAO) by d-methamphetamine (MA) in crude mitochondrial fraction isolated from whole brains of male Sprague-Dawley rats was investigated. The inhibition of MAO by various concentrations of MA was studied using serotonin (5-HT), tyramine, and phenylethylamine (PEA). Type-A MAO was shown to be active with 5-HT and norepinephrine as substrates, and to be sensitive to inhibition by a low concentration of clorgyline. Type-B MAO was shown to be active with PEA and benzylamine, and to be sensitive to inhibition by a low concentration of deprenyl. Data show that MA is a more potent inhibitor of type-A MAO than of type-B MAO. 20 references.

0004121 Suzuki, Osamu; Oya, Masakazu; Katsumata, Yoshinao. Dept. of Legal Medicine, Hamamatsu University School of Medicine, Hamamatsu 431-31, Japan **Oxidation of p-, m- and o-tyramine by type A and type B monoamine oxidase.** Biochemical Pharmacology. 28(17):2682-2684, 1979.

Tyramines were characterized as substrates for monoamine oxidase (MAO) in a crude mitochondrial fraction from male Sprague-Dawley rat brain. The susceptibility of o-tyramine deamination to clorgyline was much lower than that of p-tyramine or m-tyramine deamination. Deprenyl showed much of p-tyramine or m-tyramine deamination. Deprenyl showed much more potent inhibition for o-tyramine than for the other two. Results indicate that p-tyramine and m-tyramine are common substrates for type-A and type-B MAO, while o-tyramine is specific for type-B MAO. 24 references.

0004122 Tanaka, Toshiyuki; Starke, Klaus. Starke: Pharmakologisches Institut, Hermann-Herder-Strasse 5, D-7800 Freiburg, Germany **Antagonist/agonist-preferring alpha-adrenoceptors or alpha1/alpha2-adrenoceptors?** European Journal of Pharmacology. 63(2/3):191-194, 1980.

Yohimbine and some stereoisomeric alkaloids inhibited the binding of 3H-clonidine and 3H-WB-4101 to rat cerebral cortex membranes. Rauwolscine and yohimbine had much higher affinity for the 3H-clonidine site than for the 3H-WB-4101 site, whereas the reverse was true for corynanthine. Results indicate than the 3H-clonidine site is an alpha2-adrenoceptor and not an agonist selective site, whereas the 3H-WB-4101 site is an alpha1-adrenoceptor and not an antagonist selective site. 11 references. (Author abstract)

0004123 Tapia-Arancibia, Lucia; Arancibia, Sandor; Bluet-Pajot, Marie-Therese; Enjalbert, Alain; Epelbaum, Jacques; Priam, Mirette; Kordon, Claude. Unite 159 de Neuroendocronologie, Centre Paul Broca de l'INSERM, 2ter rue d'Alesia, F75014 Paris, France **Effect of vasoactive intestinal peptide (VIP) on somatostatin inhibition of pituitary growth hormone secretion in vitro.** European Journal of Pharmacology. 63(2/3):235-236, 1980.

Somatostatin significantly inhibited the release of growth hormone (GH) from incubated male Wistar rat hemipituitaries, but this effect was blocked by vasoactive intestinal peptide (VIP). VIP had no direct effect on GH release in vitro. Results suggest that VIP may modulate GH secretion by a direct interaction with somatostatin inhibition in the pituitary. 5 references.

0004124 Taylor, Duncan P.; Hyslop, Deborah K.; Riblet, Leslie A. Biologic Research, Mead Johnson Pharmaceutical Division, Evansville, IN 47721 **Trazodone, a new nontricyclic antidepressant without anticholinergic activity.** Biochemical Pharmacology. 29(15):2149-2150, 1980.

The anticholinergic activity of trazodone, a new nontricyclic antidepressant, was compared with other established tricyclic antidepressants via comparisons of in vitro (3H)quinuclidinyl benzilate (QNB) binding. Prevention of death after physostigmine administration was used as the in vivo estimate of activity. Trazodone was found to have much less anticholinergic activity than the tricyclic antidepressants. In addition to the clinical implications of these results, there is the suggestion that cholinergic mechanisms may have little influence on the pathophysiology and pharmacotherapy of affective illness. 9 references.

0004125 Taylor, Richard L.; Burt, David R. Dept. of Pharmacology and Experimental Therapeutics, University of Maryland School of Medicine, Baltimore, MD 21201 **Pituitary cell cultures contain muscarinic receptors.** European Journal of Pharmacology. 65(2/3):305-308, 1980.

The atropine sensitive binding of 3H-quinuclidinyl benzilate revealed the presence of muscarinic receptors in 5 day dissociated cell cultures of female Sprague-Dawley rat anterior pituitary glands. Muscarinic receptor levels in cultures were comparable to levels of receptors for dopamine and thyrotropin releasing hormone. Results suggest that muscarinic receptors are located on certain types of secretory cells and are not simply associated with vascular elements. 10 references. (Author abstract modified)

0004126 Thams, P.; Geisler, A. Dept. of Pharmacology, University of Copenhaven, 20 Juliane Maries Vej, DK-2100 Copenhagen 0, Denmark **Influence of lithium on cyclic AMP accumulation in isolated rat fat cells.** Acta Pharmacologica et Toxicologica. 45(5):329-335, 1979.

Isolated Wistar rat fat cells were used to study the effect of lithium on adenylate cyclase in vitro. In concentrations above 10mM, lithium inhibited the accumulation of cyclic AMP induced by norepinephrine or glucagon. Basal cyclic AMP content was not altered by lithium, even in concentrations as large as 40mM. The inhibitory action was time dependent and reversible, suggesting an intracellular site of action. Lithium inhibited the norepinephrine and glucagon-induced accumulation of cyclic AMP primarily in a noncompetitive fashion, but the inhibitory effect decreased with increasing hormone concentrations. Lithium and propranolol had a supraadditive effect on norepinephrine-induced cyclic AMP accumulation. It is suggested that lithium affects hormone receptor binding as well as transfer of the hormonal stimulus by an intracellular site of action. 30 references. (Author abstract modified)

0004127 Ticku, Maharaj K.; Burch, Troie. Division of Molecular Pharmacology, Dept. of Pharmacology, University of Texas Health Science Center, San Antonio, TX 78284 **Purine inhibition of (3H)-gamma-aminobutyric acid receptor binding to rat brain membranes.** Biochemical Pharmacology. 29(2):1217-1220, 1980.

Several purines, including inosine and hypoxanthine, were found to inhibit the binding of (3H)-GABA and (3H)diazepam to freeze thawed and extensively washed rat brain membranes. While purines have been reported to inhibit diazepam binding competitively, their interactions with GABA receptors in both mitochondrial and mitochondrial plus microsomal fractions are noncompetitive. The possibility that purines may bind at one site and affect the GABA receptor/ionophore/benzodiazepine complex is discussed. 30 references. (Author abstract)

0004128 Toro-Goyco, Efrain; Martin, Billy R.; Harris, Louis S. Harris: Dept. of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Binding of l-alpha-acetylmethadol and its metabolites to blood constituents.** Biochemical Pharmacology. 29(13):1897-1902, 1980.

The distribution in vitro of (-)1-alpha-acetylmethadol (LAAM) in human blood constituents, and the binding of LAAM and its metabolites to blood constituents were investigated. In concentrations close to those found in humans who are maintained on LAAM, the drug was distributed almost evenly between plasma proteins and red blood cells, but in plasma alone, over 80% was bound to protein. The major metabolites of LAAM, noracetylmethadol and dinoracetylmethadol, were also weakly and reversibly bound by serum proteins and competed with LAAM for protein binding sites. Results suggest that, assuming at least one binding site per protein molecule, the binding occurs to a protein of very low concentration in plasma. This is consistent with the data that suggest an insignificant role of human serum albumin in the binding of LAAM and the identification of a very high molecular weight protein as the possible binding entity. The data suggest that LAAM, its metabolites, and methadone compete for the same protein binding sites and that the binding capacities of plasma for both LAAM and methadone are of the same order of magnitude. Results fail to show any cooperativity on the plasma protein binding of LAAM, its metabolites or methadone. 14 references. (Author abstract modified)

0004129 Tremblay, J. P.; Grenon, G. Laboratoires de Neurobiologie, University Laval, Quebec, Canada **Benzodiazepines modify synaptic depression, frequency facilitation and PTP of an identified cholinergic synapse of Aplysia.** Life Sciences. 27(6):491-496, 1980.

Two benzodiazepines (chlordiazepoxide and flurazepam) were found to reduce the size of the excitatory postsynaptic potentials (EPSPs) produced by a cholinergic synapse and recorded in cell R15 of Aplysia californica. They also reduced the synaptic depression and the posttetanic potentiation (PTP) observed at that synapse and increased the frequency facilitation ratio. These effects of the benzodiazepines in an invertebrate are attributed to a presynaptic mechanism. They are similar to the action of GABA at that synapse but the benzodiazepines do not potentiate the action of GABA. 18 references. (Author abstract)

0004130 Tulunay, F. Cankat. Dept. of Pharmacology, Medical School of Ankara University, Sihhiye, Ankara, Turkey **The effects of morphine and various narcotic antagonist type analgesics on body temperature in rats.** Life Sciences. 27(6):511-520, 1980.

The effects of morphine, nalorphine, butorphanol, and pentazocine (narcotic antagonist type analgesics) on body temperature in rats were investigated. Morphine produced a significant hyperthermia with the doses of 5 to 160mg/kg in rats. The peak hyperthermic effect was found 1 hr after 5 to 20mg/kg doses of morphine. Nalorphine, butorphanol, and pentazocine produced biphasic effects on rectal temperature. Initially they produced a dose dependent hyperthermia and later hypothermia. In a comparison of the hyperthermic ED50s of morphine, nalorphine, butorphanol, and pentazocine, it was found that butorphanol is more active than the others. The narcotic antagonist naloxone significantly inhibited both morphine and antagonist type analgesic indiced hyperthermia. These results suggest that a different mechanism(s) is involved in the hyperthermic actions of antagonist type anlegesics and agonist drugs. 20 references. (Author abstract modified)

0004131 Tyce, Gertrude M.; Owen, Charles A., Jr. Dept. of Physiology, Mayo Clinic, Rochester, MN 55901 **Administration of L-3,4-dihydroxyphenylalanine to rats after complete hepatectomy -- I. Metabolites in tissues.** Biochemical Pharmacology. 28(22):3271-3278, 1979.

The disposition and metabolism of 14C labeled L-3,4-dihydroxyphenylalanine (L-DOPA) in plasma, erythrocytes, brain, heart, kidney, gastrointestinal tract, spleen, lung, adrenals, muscle, and pancreas were examined following i.v. injection of L-(14C)DOPA into Sprague-Dawley rats with complete hepatectomies. The total 14C in these tissues accounted for 31% of the dose in control rats and 53% in operated animals. Disproportionately high amounts of radioactivity were found in the kidney, spleen, lung, heart, and erythrocytes. Levels of (14C)dopamine were higher in most tissues of the hepatectomized rats than in controls, but the decarboxylation of DOPA appeared to be inhibited in the operated animals. Further metabolism to norepinephrine was limited in most tissues of the hepatectomized rats; most of the radioactivity was associated with 3,4-dihydroxyphenylacetic acid. Results suggest that vesicular uptake or retention of dopamine is impaired or that beta-hydroxylation is inhibited in hepatectomized animals and that most of the dopamine formed is metabolized by mitochondrial monoamine oxidase to form 3,4-dihydroxyphenylacetic acid. Monoamine oxidase did not appear to be inhibited in the hepatectomized animals. 32 references. (Author abstract modified)

0004132 Tyce, Gertrude M.; Owen, Charles A., Jr. Dept. of Physiology, Mayo Clinic, Rochester, MN 55901 **Administration of L-3,4-dihydroxyphenylalanine to rats after complete hepatectomy -- II. Excretion of metabolites.** Biochemical Pharmacology. 28(22):3279-3284, 1979.

The metabolism of 14C labeled L-DOPA in Sprague-Dawley rats with complete hepatectomies and in control rats was compared. In control animals, about 60% of the injected dose was excreted in urine and 11% in bile in 24 hours. A similar percentage of the dose (69.4%) was excreted into urine in hepatectomized animals, but the rate of excretion was slower. The decarboxylation of 14C-DOPA in 24 hours was similar in the two groups, but the metabolism of dopamine (DA) to norepinephrine was lower in the hepatectomized rats. Most of the DA was metabolized to 3,4-dihydroxyphenylacetic acid or homovanillic acid in the operated animals. 16 references. (Author abstract modified)

0004133 Tyler, Thomas Daniel. University of Kansas **Selective antagonism of the actions of amphetamine in mouse by noradrenergic uptake inhibiting agents. (Ph.D. dissertation).** Dissertation Abstracts International. 40(5):2150-B, 1979. Ann Arbor, Univ. Microfilms No. 7925878, 172p., 1979.

Central neurochemical mechanisms by which amphetamine functions were examined in the mouse by comparing the effects of noradrenergic uptake blockade upon amphetamine-induced behaviors. The effects of the in vivo amphetamine-induced depletion of endogenous norepinephrine (NE) and dopamine and tritiated NE in selected brain regions after pretreatment with nisoxetine were also observed. Nisoxetine was found to selectively inhibit the uptake of (3H)-NE, but not (3H)-dopamine or (3H)-5-hydroxytryptamine into chopped mouse brain tissue, in vitro. Pretreatment with nisoxetine selectively antagonized locomotor activity enhanced by d-amphetamine, cocaine, d-N-ethyl-amphetamine, and methylphenidate while simultaneously enhancing stereotypic behavior, in the same mouse. Nisoxetine pretreatment was compared to that with desipramine and fluoxetine. It is concluded that nisoxetine pretreatment prevents the d-amphetamine-induced depletion of NE in mouse cerebral cortex at drug dosages and with treatment schedules which correspond to those used in behavioral studies. (Journal abstract modified)

0004134 Uemura, E.; Bowman, R. E. School of Veterinary Medicine, Oregon State University, Corvallis, OR 97331 **Effects of halothane on cerebral synaptic density.** Experimental Neurology. 69(1):135-142, 1980.

A selected area of the superior sagittal cortex of 28 rats was examined for changes in synaptic density after chronic exposure to halothane. Rats were exposed to either 50, 100, or 200 ppm halothane from conception to 28 days of age. Synapses were stained with ethanolic phosphotungstic acid and morphometric measurement was carried out with a graphic digitizer. The density of cerebral synapses in rats exposed to halothane was significantly lower than those in control rats. Halothane appeared to reduce synaptic density in a linear dose dependent effect between 0 and 100 ppm of halothane. This effect appeared to plateau between 100 and 200 ppm halothane. Implications of these results for the effects of halothane on the development of synaptic organization and the maturation of synaptic contacts are discussed. 25 references. (Author abstract modified)

0004135 Vallano, Mary Lou; McIntosh, Tracy K. Memorial Sloan-Kettering Cancer Center, 1275 York Ave. (H-904), New York, NY 10021 **Morphine stimulates cholinergic neuronal activity in the rat hippocampus.** Neuropharmacology. 19(9):851-853, 1980.

High affinity, sodium dependent (3H)-choline uptake (HANDCU) into synaptosomes isolated from male Long-Evans rat hippocampus was significantly stimulated by 6mg/kg i.p. morphine, but not by a 12mg/kg dose. Pretreatment with 1mg/kg i.p. naloxone antagonized the effect of 6mg/kg morphine. Dextrophan had no effect on HANDCU. High doses of naloxone (15 and 30mg/kg) produced significant increases in HANDCU, and the effects of 30mg/kg naloxone and 6mg/kg morphine on HANDCU appeared to be additive. 8 references. (Author abstract modified)

0004136 Vargas, Froylan; Greenbaum, L.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Participation of cystein proteinase in the high affinity Ca2-dependent binding of glutamate to hippocampal synaptic membranes.** Neuropharmacology. 19(8):791-794, 1980.

Half-maximal stimulation of high affinity binding of glutamate to crude synaptic membranes from rat hippocampus was obtained with 25mcM calcium ion (Ca2). This facilitation was antagonized by leupeptin, which inhibits Ca2 dependent cystein proteinase. Results suggest that this proteinase may mediate the Ca2 dependent facilitation of glutamate binding. 11 references. (Author abstract modified)

0004137 Vendsborg, Per. Psychochemistry Instiutute, University of Copenhagen, Rigshospitalet, 9 Blegdamsvej, DK-2100 Copenhagen O, Denmark **Intravenous glucose tolerance in lithium treated rats.** Acta Pharmacologica et Toxicologica. 45(3):240-244, 1979.

A new method for performing intravenous glucose tolerance tests in anesthetized rats was developed and used to estimate glucose tolerance in female Wistar rats treated with lithium. In untreated rats, glucose tolerance increased with increasing weight and body temperature but decreased with fasting. Lithium administration increased glucose tolerance, and this increase varied with the dose and time interval between administration and glucose tolerance test. Glucose tolerance increased immediately after lithium administration, and the increase lasted for up to 25 hours, depending on the dose given and the fasting state of the animal. 21 references. (Author abstract modified)

0004138 Villanueva, L.; Pelissier, T.; Delgado, S.; Paeile, C. Dept. de Farmacologia, Facultad de Medicine Norte, Universidad de Chile, Casilla 16387 Santiago 9, Chile **Electroencephalographic effects of an anti-inflammatory analgesic: mefenamic acid.** Research Communications in Chemical Pathology and Pharmacology. 26(2):253-262, 1979.

Mefenamic acid produced a progressive and dose related increase in the voltage of baseline EEG patterns in rats and cats. Baseline activity was restored within 15 minutes after low doses and within 30 minutes after high doses. Cats showed greater sensitivitiy to the drug than rats. Naloxone did not modify the EEG effects of mefenamic acid in either species. It is concluded that mefenamic acid in exerts short lasting ventral depressant effects at low doses and stimulant or facilitatory effects at high doses. 5 references. (Author abstract modified)

0004139 Walker, John Michael. Ohio State University **ACTH and central mechanisms of pain inhibition. (Ph.D. dissertation).** Dissertation Abstracts International. 40(4):1942-B, 1979. Ann Arbor, Univ. Microfilms No. 7922576, 69p., 1979.

The connection between ACTH and central mechanisms of pain inhibition was studied. Org 2766, an analog of adrenocorticotropic hormone 4-9, was injected into the central gray of rats. Profound analgesia was observed at doses of 9.5 and 30mcg for up to 30 mintues, but similar injections into the lateral ventricles produced no analgesia. These results suggest that the central gray is the site of action of Org 2766. Naloxone HCl, administered subcutaneously, did not significantly shorten the duration of analgesia induced by injections of the analog into the periaqueductal gray. Moreover, Org 2766 was found to only weakly inhibit the binding of 3H-leu-enkephalin to opiate receptors. It is concluded that the behavioral effects of Org 2766 are not medi-

ated by opiate receptors. It is also suggested that since beta-endorphin and ACTH apparently reside within the same cells, ACTH may by important in the central inhibition of pain. (Journal abstract modified)

0004140 Walker, Richard F. Dept. of Anatomy, University of Kentucky Medical Center, Lexington, KY 40506 **Serotonin neuroleptics change patterns of preovulatory secretion of luteinizing hormone in rats.** Life Sciences. 27(12):1063-1068, 1980.

Serotonin receptor agonists or antagonists were employed to determine the timing and influence of serotonergic neurotransmission on phasic secretion of luteinizing hormone (LH). Daily injections of cyproheptadine (CP) or methysergide (MS), serotonin antagonists, initiated at 1600 h on the day of vaginal proestrus, blocked the LH surge and ovulation. Vaginal smears remained cornified for 2 to 3 days. The drugs were ineffective when given at 0800 h, though they terminated the LH surge prematurely when administered at 1730h. When quipazine, a serotonin receptor agonist was injected at 1400 h or 2000 h on proestrus, serum LH levels rose. This effect caused the LH surge to begin prematurely or to be sustained unusually long. Quipazine injected on diestrus two did not cause LH levels to rise, suggesting that its effect is estrogen dependent. Serotonin turnover in the hypothalamus was greater during onset of the LH surge than during its termination. Results indicate that phasic secretion of LH on proestrus is accompanied by and may be dependent upon a period of serotonin neural activity. 15 references. (Author abstract modified)

0004141 Waller, Marshall B.; Richter, Judith A. Richter: Institute of Psychiatric Research, Indiana University School of Medicine, 1100 West Michigan St., Indianapolis, IN 46223 **Effects of pentobarbital and Ca2 on the resting and K-stimulated release of several endogenous neurotransmitters from rat midbrain slices.** Biochemical Pharmacology. 29(16):2189-2198, 1980.

The release of endogenous amino acides (GABA, glutamate, aspartate, glycine and alanine) and of 5-hydroxtryptamine (5-HT) and acetylcholine (ACh) from rat midbrain slices was examined under various conditions of superfusion. Depolarization with high K stimulated the release of all substances examined, but the K stimulated release was Ca2 dependent only for GABA, glutamate, aspartate, 5-HT, and ACh. Pentobarbital, although not substantially affecting resting release, inhibited the K stimulated release of GABA, glutamate, aspartate, and ACh markedly and significantly. The effect of pentobarbital on K stimulated 5-HT release was not statistically significant. These results are consistent with the hypothesis that the barbiturate inhibits stimulated transmitter release by inhibiting Ca2 influx during depolarization. 67 references. (Author abstract modified)

0004142 Wielosz, M.; Przegalinski, E.; Kleinrok, Zd. Dept. of Pharmacology, Institute of Clinical Pathology, Medical Academcy, 20090 Lublin, Poland **In vivo effect of danitracen on the uptake mechanism in monoaminergic neurons and platelets in rats.** Agressologie. 20(D):253-257, 1979.

The effect of danitracen on depletion of 5-HT and catecholamines in the brain and platelets of rats was studied. Danitracen in a dose of 10mg/kg significantly antagonized the depletion of brain and platelet 5-HT produced by p-chloroamphetamine and the depletion of brain 5-HT induced by fenfluramine. Similar but stronger effects were observed ater chlorimipramine. On the other hand, danitracen seemed to have no effect on depletion of brain catecholamines induced by 6-OHDA, while desipramine significantly antagonized decrease of noradrenaline. Danitracen also had no effect on the depletion of brain and platelet 5-HT produced by reserpine. These findings indicate that danitracen is a selective but weak inhibitor of 5-HT uptake in rat brain and platelets. 23 references. (Author abstract modified)

0004143 Williams, Michael; Risley, Edwin A. Neuropsychopharmacology Section, Merck Institute for Therapeutic Research, West Point, PA 19486 **High affinity binding of 2-chloroadenosine to rat brain synaptic membranes.** European Journal of Pharmacology. 64(4):369-370, 1980.

The binding of tritiated 2-chloroadenosine (3H-CADO) to crude synaptic membranes from rat brain was studied. Results revealed the presence of a specific, high affinity, theophylline sensitive purinergic binding site. Binding was not significantly altered by phentolamine, d-propranolol, spiroperidol, naloxone, methysergide, atropine, diazepam, adenine, inosine, or hypoxanthine. 5 references.

0004144 Woelk, H. Universitats-Nervenklinik, Einheit fur Neurochemie Universitat Erlangen, Schwabachanlage 6, D-8520 Erlangen, Germany **Effects of Piracetam on the incorporation of 32P into the phospholipids of neurons and glial cells isolated from rabbit cerebral cortex.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(3):251-256, 1979.

The biochemical basis of the action of Piracetam was investigated, via an examination of the effects of the drug on neuronal and glial phospholipids isolated from rabbit cerebral cortex. Results show that Piracetam increased the incorporation of 32P into phosphatidylinositol and phosphatidyl choline of both glia and neuronal cell bodies. Glial cells contained approximately one third more phospholipids per unit protein than neuronal cell bodies. The distribution and pattern of phospholipid relative to the total amount, was similar in both cell types. Results suggest that Piracetam stimulates excitatory neurons and may be involved in the process of synaptic transmission. The stimulatory effect of Piracetam on the incorporation of 32P into phosphatidylinosital and phosphatidyl choline appeared to be mediated by norepinephrine or another neurotransmitter. 26 references. (Author abstract modified)

0004145 Wong, Gordon B.; Sellers, Edward M. Clinical Pharmacology Program, Addiction Research Foundation, Clinical Institute, Toronto, Ontario, Canada M5S 2S1 **Intravascular factors affecting diazepam binding to human serum albumin.** Biochemical Pharmacology. 28(22):3265-3270, 1979.

The effects of fatty acids, uric acid, bilirubin, desmethyldiazepam, and oxazepam on the binding of diazepam to defatted human serum albumin were studied by equilibrium dialysis. Oleic acid decreased the binding of diazepam at all molar ratios of fatty acid. In contrast, palmitic acid at ratios of less than 1:1 enhanced diazepam binding. Uric acid and bilirubin had negligible effects on binding. Diazepam binding was greater than that of desmethyldiazepam or oxazepam, and both metabolites reduced diazepam binding to albumin. Results suggest that differences in the absolute ratio of specific fatty acids to each other may account for interindividual variations in diazepam binding observed in vivo. 28 references. (Author abstract modified)

0004146 Wood, J. D.; Hertz, L. Dept. of Biochemistry, University of Saskatchewan, Saskatoon, Saskatchewan, Canada S7N OWO **Ketamine-induced changes in the GABA system of mouse brain.** Neuropharmacology. 19(8):805-808, 1980.

Intramuscular injection of 0.8mma-l/kg ketamine in male Swiss mice induced a significant increase in GABA content in whole brain and in synaptosome enriched fractions prepared from whole brain. Addition of 0.25 to 1.0mM ketamine to the incubation medium inhibited the uptake of GABA by synaptosome enriched fractions and cultured astrocytes and neurons; the inhibition was greatest for neurons and least for synapto-

somes. It is suggested that the anesthetic and anticonvulsant properties of ketamine may be due to an accumulation of GABA in the synaptic cleft, brought about by inhibition of GABA uptake into glia and neuronal perikarya. 13 references. (Author abstract modified)

0004147 Wuster, M.; Duka, Theodora; Herz, A. Dept of Neuropharmacology, Max-Planck-Institute fur Psychiatrie, Kraepelinstrassee 2, D-8000 Munich 40, Germany **Diazepam effects on striatal met-enkephalin levels following long-term pharmacological manipulations.** Neuropharmacology. 19(6):501-505, 1980.

As measured by highly specific radioimmunoassay, long-term treatment of rats for 28 days with benzodiazepines resulted in a significant increase in the striatal met-enkephalin content, which was opposite to the decrease in this area observed after acute administration. Other areas investigated, i.e., the hypothalamus, the medulla oblongata/pons and the midbrain were unchanged after chronic benzodiazepine treatment. Acute diazepam challenge of these animals revealed a considerable degree of tolerance towards the acute drug effect. In rats chronically treated with morphine for 28 days, acute diazepam administration no longer decreased striatal met-endephalin, in contrast to rats receiving ethanol for the same time, in which the diazepam-induced decrease was potentiated. 24 references. (Author abstract)

0004148 Yamada, Shizuo; Yamamura, Henry I.; Roeske, William R. Roeske: Dept. of Internal Medicine, University of Arizona Health Sciences Center, Tucson, AZ 85724 **The regulation of cardiac alpha/adrenergic receptors by guanine nucleotides and by muscarinic cholinergic agonists.** European Journal of Pharmacology. 63(2/3):239-241, 1980.

Guanyl-5'-yl imidodiphosphate selectively decreased the affinity of male Sprague-Dawley rat cardiac alpha1-adrenoceptors for the agonist (-)-epinephrine. This effect was partially reversed by the muscarinic cholinergic agonist carbachol. This biochemical evidence suggests that muscarinic cholinergic agonists can regulate the affinity of cardiac alpha1-adrenoceptors by modulating the effect of guanyl nucleotides. 5 references.

0004149 Yamamoto, M.; Murayama, S. Research Laboratories, Yamanouchi Pharmaceutical Co. Ltd., Azusawa, Itabashi-ku, Tokyo 174, Japan **Effect of the serotonergic system on the caudate nucleus.** Pharmacology. 20(6):310-315, 1980.

The effects of L-5-hydroxytryptophan (L-5HTP), an active precursor of 5-hydroxytryptamine (5-HT), and electrical stimulation of the dorsal raphe nucleus were observed on the activity of the caudate nucleus in cats via EEG and evoked potential methods. In an EEG study, the caudate spindle and the VA spindle, recorded in the cerebral cortex and induced by electrical stimulation of the caudate nucleus and the anterior ventral nucleus, respectively, were inhibited by L-5HTP. The inhibitory effect of L-5HTP on the caudate spindle was stronger than that on the VA spindle. These inhibitory effects of L-5HTP were observed when L-5HTP showed synchronization on spontaneous EEG and no effect on the duration of the cortical afterdischarge. In the evoked potential study, both electrical stimulation of the dorsal raphe nucleus and exogenous L-5HTP inhibited the activity of the potentials in the caudate nucleus induced by electrical stimulation of the radial nerve. These results suggest that the neuronal activity of the caudate nucleus is inhibited by the serotonergic system. 14 references. (Author abstract)

0004150 Yanai, Joseph; Tabakoff, Boris. Dept. of Anatomy and Embryology, Hebrew University-Hadassah Medical School, P.O. Box 1172, Jerusalem, Israel **Increased tolerance in mice following prenatal exposure to barbiturate.** Psychopharmacology. 64(1):325-327, 1979.

The effects of in utero exposure to phenobarbital (PhB) on initial sensitivity to the hypnotic effects of barbiturates and on the rate of development of functional (CNS) tolerance to barbiturates were investigated in mature rats. HS/Ibg (heterogeneous stock) mice dams were fed milled mouse food containing 3g/Kg PhB in acid form and water as their only nutritional source from gestation days 9 to 19. Control females received milled food and water. Blood PhB levels of treated females and fetuses were 40 to 200mg/ml blood. At the age of 50 days, male offspring were injected with C14 sodium pentobarbital (PenB). Sleep time and temperature loss were monitored and, in randomly selected individuals, brain PenB levels were determined upon awakening. The experiment was repeated on the same animals for 3 consecutive days. All offspring developed functional (CNS) tolerance during the 3 testing days as evidenced by the daily decrease in sleep time while brain levels of PenB upon awakening increased. Offspring who received PhB prenatally had generally shorter sleep times, less temperature loss, and higher brain PenB levels upon awakening than controls. The differences were most pronounced on the second day. 13 references. (Author abstract modified)

0004151 Yarbrough, G. G.; Singh, D. K. Merck Institute for Therapeutic Research, West Point, PA 19486 **Effects of MK-771 on the isolated amphibian spinal cord: comparison with thyrotropin-releasing hormone.** Canadian Journal of Physiology and Pharmacology. 57(8):920-922, 1979.

A novel thyrotropin releasing hormone (TRH) analogue, pyro-2-aminoadipyl-histidyl-thiazolidine-4-carboxamine (MK-771), was equipotent with TRH in depolarizing the ventral roots of the isolated, hemisected amphibian spinal cord. The 3-methyl-mistidyl analogue of TRH was about 10 times more potent than MK-771 and TRH. Since TRH and MK-771 are also equipotent in the pituitary, results suggest that the enhanced potency of MK-771 relative to TRH in the CNS in vivo is not due to difference in the agonist requirements of CNS and pituitary TRH receptors. 9 references. (Author abstract modified)

0004152 Yen, Mao-Hsiung; Ku, Pei-Yu; Lee, Hsheng-Kai. Dept. of Pharmacology, National Defense Medical Center, Taipei, Taiwan **The effect of (D-Ala2)-met-enkephalin on the contraction of nictitating membrane in cats.** European Journal of Pharmacology. 63(2/3):213-216, 1980.

The nictitating membrane contraction induced by cervical sympathetic nerve stimulation in anesthetized cats was greatly reduced by pretreatment with (D-Ala2)-Met-enkephalin (DAME, 300mcg/kg i.v.), and the DAME effect was readily reversed by naloxone (1mg/kg i.v.). However, DAME had no effect on nictitating membrane contractions induced by i.v. application of norepinephrine (NE). Cocaine potentiated contractions induced by sympathetic nerve stimulation or NE, but DAME suppressed the effects of cocaine only on contractions induced by nerve stimulation. It is concluded that DAME has a morphine-like effect on contraction of the nictitating membrane. 5 references. (Author abstract modified)

0004153 Zaprianov, Z.; Bainova, A. Institute of Hygiene and Occupational Health, Boulv. D. Nestorov 15, 1431 Sofia, Bulgaria **Changes in monoamine oxidase activity (MAO) after styrene and ethanol combined treatment of rats.** Activitas Nervosa Superior. 21(4):262-265, 1979.

Changes in monoamine oxidase activity (MAO) after combined styrene and ethanol treatment of rats are described. Males rats were orally administered styrene, ethanol, or styrene plus ethanol for 7 days and MAO activity was determined in the serum, liver, and brain homogenates. Styrene administration resulted in marked MAO inhibition in brain, less pronounced re-

ductions in liver, and nonsignificant effects in serum. The inhibition of the MAO activity in total brain is viewed as a possible link in the pathogenesis of occupational neurophysiological effects of styrene. Ethanol consumption increased the adverse action of styrene on MAO activity, and may be related to deviations in brain neurotransmitter metabolism and/or the styrene biotransformation. 8 references.

0004154 Zieher, Luis Maria; Jaim-Etcheverry, Guillermo. Jaim-Etcheverry: Instituto de Biologia Celular, Facultad de Medicina, Paraguay 2155, 1121 Buenos Aires, Argentina **Neurotoxicity of N-(2-choloroethyl)-N-ethyl-2-bromobenzylamine hydrochloride (DSP 4) on noradrenergic neurons is mimicked by its cyclic aziridinium derivative.** European Journal of Pharmacology. 65(2/3):249-256, 1980.

Endogenous noradrenaline (NA) levels were measured in the brain and heart of female BALBc mice after injection of N-(2-chloroethyl)-N-ethyl-2-bromobenzylamine hydrochloride (DSP-4) immediately after the neurotoxin was dissolved or after the compound was incubated under conditions that promote its conversion to an aziridinium derivative. The incubated compound depleted NA in the CNS when injected directly into the brain, but had only peripheral effects when injected i.p. Pretreatment with the uptake blocker desmethylimipramine blocked the effects of DSP-4 and its aziridinium derivative. 15 references. (Author abstract modified)

0004155 Zimmer, G.; Gross, W.; Mehler, U.; Dorn-Zachertz, D. Gustav-Embden-Zentrum, Theodor-Stern-Kai 7, D-6000 Frankfurt/Main 70, Germany **Membrane action of tricyclic drugs: influence on amino acid transport in Streptomyces hydrogenans and on lipid transition temperature in red blood cell membranes.** Arzneimittel-Forschung. 30(2):221-228, 1980.

The influence of tricyclic drugs on amino acid transport in Streptomyces hydrogenans cells and on red cell membrane lipid transition was investigated by different methods, including viscosimetry, 90 degree light scattering measurements, and 1-anilinonaphthalene-8-sulfonate fluorescence. Results indicate that fluphenazine and thioridazine primarily interact with the hydrophobic part of the membrane lipid constitutents intercalating between the hydrocarbon chains. In contrast, amitriptyline and doxepine are considered to mainly interact with the hydrophilic part of the membrane (lipid) constituents. Concomitant interaction with membrane proteins and/or lipid protein interaction is not ruled out for these four drugs. 29 references. (Author abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

004156 Albertson, T. E.; Peterson, S. L.; Stark, L. G. Dept. of Pharmacology, School of Medicine, University of California, Davis, CA 95616 **Anticonvulsant drugs and their antagonism of kindled amygdaloid seizures in rats.** Neuropharmacology. 19(7):643-652, 1980.

The effects of 20 drugs known to have anticonvulsant properties and two new compounds were studied in Sprague-Dawley rats kindled by amygdaloid stimulation. Barbiturates, benzodiazepines, a piperazine, an acetate derivative, and WB-CPI (a significantly modified phenacylurea) were the most effective in attenuating the kindled seizures. Results indicate that kindled amygdaloid seizures in the rat provide a model of epilepsy useful for detecting compounds with anticonvulsant activity. 35 references. (Author abstract modified)

004157 Alexander, George J.; Kopeloff, Lenore M.; Alexander, Rita B. New York State Psychiatric Institute, New York, NY 10032 **6-Hydroxydopamine and metrazol seizures in mice: inhibition of the tonic-clonic phase.** Neuropharmacology. 19(7):679-681, 1980.

Pretreatment with 6-hydroxydopamine (6-OHDA, 43 or 50mg/kg i.p.) markedly altered seizure responses to metrazol (82mg/kg i.p.) in CF-1 mice. The incidence of myoclonic features was not altered by 6-OHDA, but the clonic/tonic component was completely abolished. Results indicate that 6-OHDA blocks the propagation of seizures without affecting the initiation of neuronal excitation. 8 references. (Author abstract modified)

004158 Allen, R. Michael; Lane, John D.; Brauchi, John T. Dept. of Psychiatry, Louisiana State University Medical Center, P. O. Box 33932, Shreveport, LA 71130 **Amantadine reduces haloperidol-induced dopamine receptor hypersensitivity in the striatum.** European Journal of Pharmacology. 65(2/3):313-315, 1980.

The development of striatal dopaminergic receptor hypersensitivity normally observed after chronic haloperidol treatment was greatly reduced by amantadine hydrochloride. Maximal 3H-spiroperidol receptor binding and apomorphine-induced stereotypy were both reduced in rats treated with haloperidol (5mg/kg ip) and amantidine (50mg/kg ip) for 21 days, compared to those treated with haloperidol alone. Results suggest that amantidine may prevent the development of tardive dyskinesia in humans treated chronically with neuroleptics. 8 references. (Author abstract modified)

004159 Anika, S. M.; Houpt, T. R.; Houpt, K. A. Dept. of Physiology, Biochemistry, and Pharmacology, New York State College of Veterinary Medicine, Cornell University, Ithaca, NY 14853 **Insulin as a satiety hormone.** Physiology & Behavior. 25(1):21-23, 1980.

The effects of small doses of insulin on food intake were examined in 11 pigs (1 to 3 months old, 5 to 50kg) fitted with intrajugular catheters. After a 4 hours fast, insulin was injected and food intake was measured for 10 minutes. The dose/response curve was U-shaped; food intake was significantly depressed after 0.05, 0.13, and 0.25U/kg, but not after 0.03, 0.5, or 1.OU/kg. It is suggested that endogenous insulin release may induce a rapid satiety effect. 11 references. (Author abstract modified)

004160 Anisman, Hymie; Remington, Gary; Sklar, Lawrence S. Dept. of Psychology, Carleton University, Ottawa, Ontario, K1S 5B6, Canada. **Effect of inescapable shock on subsequent escape performance: catecholaminergic and cholinergic mediation of response initiation and maintenance.** Psychopharmacology. 61(2):107-124, 1979.

Catecholaminergic and cholinergic mediation of response initiation and maintenance were examined in a study of the effect of inescapable shock on subsequent escape performance in mice. Following exposure to inescapable shock, subsequent escape performance is disrupted if the task is one in which animals receive forced exposure to shock for several seconds before escape is possible. The extent of the deficit is directly related to the severity of the initial stress and the duration of escape delay used during test. Treatment with a tyrosine hydroxylase inhibitor, alpha-methyl-p-tyrosine; a dopamine beta-hydroxylase inhibitor, FLA-63; or dopamine antagonists, haloperidol, and pimozide mimicked the effects of inescapable shock in the different escape paradigms. The effects of haloperidol were antagonized by treatment with scopolamine. As observed in the case of inescapable shock, prior escape training abated the disruptive effects of the drug treatments. Finally, decreasing or blocking catecholamine activity or increasing cholinergic activity exacerbated the effect of a moderate amount of inescapable shock on subsequent escape performance. These treatments also induced reduc-

tions in shock elicited activity. Conversely, treatment with L-dopa, or scopolamine antagonized the reduction in shock elicited activity and the escape deficits engendered by prior inescapable shock. It is hypothesized that both dopamine and norepinephrine, as well as acetylcholine are involved in the escape deficit observed after inescapable shock, and that these transmitters mediate the interference by their influence on response initiation and maintenance, rather than on associative or cognitive processes.

004161 Arnone, M.; Dantzer, R. INRA, Station de Pharmacologie, 180 chemin de Tournefeuille, F-31300 Toulouse, France **Effects of diazepam on extinction-induced aggression in pigs.** Pharmacology Biochemistry and Behavior. 13(1):27-30, 1980.

The effects of diazepam (1 to 2mg/kg) on extinction-induced aggression in pigs were studied. Pairs of pigs were trained to press a panel for food. Diazepam enhanced resistance to extinction but did not alter agression when access to the response panel and feeding was permitted. When such access was denied, however, diazepam increased the severity of aggression observed between animals. Plasma corticosteroid levels were depressed in all the diazepam treated pigs. Results suggest that benzodiazepines induced a response persistence syndrome rather than acting on frustration or agressiveness per se. 19 references. (Author abstract modified)

004162 Arnt, Jorn; Scheel-Kruger, Jorgen. Psychopharmacological Research Laboratory, Dept. E, Sct. Hans Mental Hospital, DK-4000 Roskilde, Denmark **GABAergic and glycinergic mechanisms within the substantia nigra: pharmacological specificity of dopamine-independent contralateral turning behavior and interactions with other neurotransmitters.** Psychopharmacology. 62(3):267-277, 1979.

The specificity of dopamine independent behavioral stimulation and some possible interactions between nigral GABAergic systems and other nigral and striatal/limbic neurotransmitter systems were investigated with male Wister SPF rats. Muscimol-induced turning was antagonized by intranigral bicuculline methochloride (BMC) and picrotoxin, whereas antagonists of glycine, morphine, dopamine, noradrenaline, and serotonin were ineffective. Glycine induced a qualitatively similar turning behavior which was strychnine sensitive but relatively BMC and picrotoxin insensitive. Results suggest specificity of GABA agonist induced contralateral turning and indicate an interaction between nigral GABA and other neurotransmitters, particularly dopamine and acetylcholine. 52 references. (Author abstract modified)

004163 Ashorobi, R. B.; Guha, D.; Pradhan, S. N. Dept. of Pharmacology, College of Medicine of the University of Lagos, P.M.B. 12003, Lagos, Nigeria **Electrophysiological correlates of the behavioral effects of tubocurarine in conscious cats.** Psychopharmacology. 64(3):349-353, 1979.

The effects of tubocurarine on behavior, electrical activity, and auditory evoked potentials were studied in restrained conscious cats. Tubocurarine hydrochloride produced various central stimulatory effects characterized by EEG desynchronization, decrease in both low and high alpha waves, and decrease in the amplitude and area of the suface positive (P1) wave of auditory evoked potentials. Concomitant with the alterations in brain electrical activity, tubocurarine hydrochloride produced generalized behavioral arousal phenomena and the cats became restless and exhibited miaowing and increased movement of the head and ears. Almost all parameters except behavior showed a distinct dose response relationship. A correlation between the behavioral effects and the EEG analog was thus demonstrated. 18 references. (Author abstract)

004164 Aulakh, C. S.; Ghosh, B.; Pradhan, S. N. Pradhan: Dept. of Pharmacology, College of Medicine, Howard University, Washington, DC 20059 **Actions and interactions of cocaine on self-stimulation behavior in rats.** Psychopharmacology. 63(1):75-79, 1979.

The effect of cocaine, over a dose range of 2 to 60mg/kg, i.p., on self-stimulation (SS) behavior was studied in rats with electrodes either in the posterior hypothalamus (PH, monoaminergic) or the area ventralis tegmentum (A10, dopaminergic). The drug increased SS behavior with peak effects at 30mg/kg in PH rats and 20mg/kg in A10 rats. Azaperone (an alpha adrenergic blocker) and haloperidol (an antidopaminergic neuroleptic) given at doses that did not affect baseline SS responses reduced cocaine-induced enhancement of SS in both PH and A10 rats, showing the involvement of both noradrenergic and dopaminergic mechanisms in SS behavior. A scopolamine dose that itself facilitated SS responding enhanced the effect of cocaine on this behavior, thus suggesting an additional involvement of cholinergic mechanism in cocaine effect. 26 references. (Author abstract)

004165 Avis, Harry H.; Peeke, Harman V. S. Antioch University, 650 Pine Street, San Francisco, CA 94108 **The effects of pargyline, scopolamine, and imipramine on territorial aggression in the convict cichlid (Cichlasoma nigrofasciatum).** Psychopharmacology. 66(1):1-2, 1979.

The effects of pargyline scopolamine, and imipramine on territorial aggression in the convict cichlid (Cichlasoma nigrofasciatum) were investigated. Scopolamine, pargyline, and imipramine reduced territorial aggression. Imipramine was effective at much lower doses than either scopolamine or pargyline. None of the drugs affected activity or predation/feeding, indicating that the observed drug effects are relatively specific. The ineffectiveness of methyl scopolamine suggests that the cholinergic effect is centrally mediated, since in most species methyl scopolamine is less effective centrally than socoplamine. 5 references. (Author abstract modified)

004166 Bailey, Ruth C.; Jackson, C. M.; Bracs, P.U. Jackson: Dept. of Pharmacology, University of Sydney, New South Wales 2006, Australia **Long-term L-Dopa pretreatment of mice: central receptor subsensitivity or supersensitivity?** Psychopharmacology. 66(1):55-61, 1979.

The effect of acute and repeated treatments with L—dopa in oral doses of 100mg/kg plus benserazide (50mg/kg) was studied using locomotor activity in mice as a model of central catecholaminergic function. Mice pretreated with L-Dopa once daily for 1,4, or 10 days responded to a challenge dose of L-Dopa 1 day later with a more pronounced increase in motor activity than vechicle pretreated animals. Dexamphetamine-induced stimulation was not significantly different in the two pretreatment groups when mice were challenged 1 day after one or four pretreatment doses of L-Dopa. However, a reduced response to dexamphetamine was observed in L-Dopa pretreated mice (compared to vehicle treated mice) on withdrawal of the mice from a 10 day L-Dopa pretreatment schedule. One day after one L-Dopa dose, with or without premedication with alpha-methyl-tyrosine plus reserpine, mice responded to apomorphine with significantly less activity than vehicle pretreated mice. In contrast, 1 day after 10 doses of L-Dopa, there was a shift to the left of the dose/response curve to apomorphine, which did not, however, occur 4 days after withdrawal. Hence, marked dopamine receptor sensitivity changes seem not to be of primary importance for L-Dopa hyperactivity in L-dopa pretreated mice. Results also suggest that dopaminergic changes are not of consequence in the activity induced by dexamphetamine in L-

Dopa pretreated animals. 24 references. (Author abstract modified)

004167 Balsara, J. J.; Jadhav, J. H.; Muley, M. P.; Chandorkar, A. G. Dept. of Pharmacology, V. M. Medical College, Solapur (Maharashtra) 413003, India **Effect of drugs influencing central serotonergic mechanisms on methamphetamine-induced stereotyped behavior in the rat.** Psychopharmacology. 64(3):303-307, 1979.

The effects of drugs influencing central serotonergic mechanisms on methamphetamine-induced stereotyped behavior in rats were investigated. Pretreatment with L-tryptophan, a precursor of serotonin, was found to decrease the intensity of stereotyped behavior induced by methamphetamine while methysergide, a serotonin antagonist was found to increase the intensity of methamphetamine-induced stereotyped behavior. These results suggest that the intensity of methamphetamine-induced stereotypy depends on the balance between central dopaminergic and serotonergic systems and that the central serotonergic system amy have an opposing, tonic effect upon central dopaminergic systems involved in the mediation of stereotypy. In contrast to L-tryptophan, however, pretreatment with quipazine, a serotonin agonist, and blocker, was found to potentiate the stereotyped behavior induced by methamphetamine. The probable mechanisms by which quipazine and clomipramine might have potentiated the methamphetamine-induced stereotypy are discussed. 32 references. (Author abstract modified)

004168 Bareggi, S. R.; Becker, R. E.; Ginsburg, B.; Genovese, E. Istituto di Farmacologia, IV Cattedra, Facolta di Medicina, Universita di Milano, Via Vanvitelli 32, I-20129 Milan, Italy **Paradoxical effect of amphetamine in an endogenous model of the hyperkinetic syndrome in a hybrid dog: correlation with amphetamine and rho-hydroxyamphetamine blood levels.** Psychopharmacology. 62(3)217-224, 1979.

The relationships between behavioral responses (behavior, hyperthermia, and inhibitory training) of telomian-beagle hybrids and beagles to d-amphetamine and the blood levels of amphetamine and its metabolite rho-hydroxyamphetamine (rho-OA) were examined. Behavior tests showed that hybrids, like children, exhibit hyperactivity, impulsiveness, and impaired learning. Two groups of hybrids could be differentiated; the behavior of one improved after amphetamine (responders) while that of the other did not (nonresponders). Hybrids were less responsive than beagles to other effects of amphetamine such as stereotyped behavior and hyperthermia. Measurements of blood levels showed that hybrids form less rho-OA. It is suggested that the lesser response of hybrids to toxic effects of amphetamine is due to this difference in amphetamine metabolism. 13 references. (Author abstract modified)

004169 Bauer, Richard H. Dept. of Psychology, Kansas State University, Manhattan, KS **The effects of l-, d-, and parahydroxy-amphetamine on locomotor activity and wall climbing in rats of different ages.** Pharmacology Biochemistry and Behavior. 13(2): 155-165, 1980.

The behavioral effects of amphetamine (0.5 to 16mg/kg) were studied in male Sprague-Dawley rats at 15, 17, 21, 36, 90, and 275 days of age. Low doses of l-amphetamine caused a greater increase in photocell crossing than high doses at 15 days of age, but the dose response curve gradually shifted toward higher doses by day 36. D-amphetamine had a greater effect than l-amphetamine on adult locomotion, but l-amphetamine was more potent at some points during development. Low doses of both amphetamine isomers increased wall climbing at the three youngest ages, but higher doses had no effect; a 4mg/kg dose of d-amphetamine slightly increased wall climbing at 36 days of age, but no dose of either isomer altered wall climbing in adults. Parahydroxy-amphetamine, which has only peripheral effects, did not significantly alter locomotor or wall climbing behavior. 28 references. (Author abstract modified)

004170 Baum, Michael J.; Starr, Matthew S. Massachusetts Institute of Technology, Room 37-315, Cambridge, MA 02139 **Inhibition of sexual behavior by dopamine antagonist or serotonin agonist drugs in castrated male rats given estradiol or dihydrotestosterone.** Pharmacology Biochemistry and Behavior. 13(1):57-67, 1980.

Studies in Long-Evans rats suggested that the testosterone metabolites estradiol (E2) and 5 alpha-dihydrotestosterone (DHT) may contribute to the activation of masculine sexual behavior by enhancing dopaminergic neurotransmission and suppressing serotonergic transmission. The dose of the dopamine receptor blocker spiperone needed to significantly reduce mounting and intromission was lower in castrated males implanted with silastic capsules containing E2 than in those implanted with DHT. The dopamine receptor blocker clozapine was equally effective in suppressing male sexual behavior in castrated rats implanted with E-2 or DHT as was the serotonin reuptake blocker fluoxetine. The serotonin receptor agonist 5-methoxy-N, N-dimethyltryptamine showed no suppressive effects in either group. 47 references (Author abstract modified)

004171 Bedford, John A.; Borne, Ronald F.; Wilson, Marvin C. Research Institute of Pharmaceutical Sciences, University of Mississippi, University, MS 38677 **Comparative behavioral profile of cocaine and norcocaine in rats and monkeys.** Pharmacology Biochemistry and Behavior. 13(1):69-75, 1980.

Studies in two species showed that the cocaine metabolite norcocaine is pharmacologically active. In male Wistar rats, cocaine and norcocaine both significantly reduced food consumption and decreased responding on a fixed ratio schedule of food reinforcement. Cocaine increased fixed interval (FI) responding at 10, 20, and 40mg/kg; norcocaine had no effect at the low dose and decreased FI responding at 20 and 40mg/kg. Cocaine significantly increased locomotor activity at these doses, but produced convulsions and death at 60 and 80mg/kg. Cocaine (0.2mg/kg) and norcocaine (0.5, 0.2, and 0.8mg/kg) both maintained i.v. self-administration in rhesus monkeys. 19 references. (Author abstract modified)

004172 Beleslin, D. B.; Samardzic, Ranka. Dept. of Pharmacology, Medical Faculty, P.O. Box 662, Belgrade 11000, Yugoslavia **Evidence of central cholinergic mechanisms in the appearance of affective aggressive behaviour; dissociation of aggression from autonomic and motor phenomena.** Psychopharmacology. 62(2):163-167, 1979.

Evidence was sought of central cholinergic mechanisms in the appearance of affective behavior in cats. Carbachol, muscarine, eserine and neostigmine injected into the cerebral ventricles of conscious cats evoked emotional phenomena as well as clonic/tonic convulsions. After intraventricular hemicholinium-3 and triethylcholine carbachol, muscarine, eserine and neostigmine elicited autonomic and motor phenomena. Choline administered into the cerebral ventricles of hemicholinium-3 and triethylcholine treated cats restored the emotional behavior with aggression, autonomic and motor phenomena as well as clonic/tonic convulsions to intraventricular carbachol, muscarine, eserine and neostigmine. It is concluded that cholinergic neurons are involved in the appearance of the affective type of aggression resulting from intraventricular carbachol, muscarine, eserine and neostigmine. 18 references. (Author abstract modified)

004173 Beleslin, D. B.; Samardzic, Ranka. Dept. of Pharmacology, Medical Faculty, P.O. Box 662, Belgrade 11000, Yugosla-

via **Effects of 6-hydroxydopamine and reserpine on aggressive behavior induced by cholinomimetic and anticholinestrase injections into cerebral ventricles of conscious cats: dissociation of biting attack from snarling and hissing.** Psychopharmacology. 61(2):149-153, 1979.

To further examine the role of central catecholamine and 5-hydroxytryptamine neurons on affective type aggressive behavior, the effects of carbachol, muscarine, eserine, and neostigmine on 6-hydroxydopamine and reserpine treated cats were examined. Carbachol, muscarine, eserine, and neostigmine, injected into the cerebral ventricles of control conscious cats evoked emotional behavior with aggression, autonomic, and motor phenomena with clonic/tonic convulsions. The most impressive feature of the gross behavioral effects on intraventricular cholinomimetics and anticholinestrase was affective type aggression. Intraventricular 6-hydroxydopamine and reserpine, as well as parenterally administered reserpine, carbachol, muscarine, eserine, and neostigmine, elicited aggression, autonomic, and motor phenomena with clonic/tonic convulsions. Of affective aggressive behavior, the biting attack was the most apparent, while hissing and snarling (i.e., vocalization) were depressed or absent. The most resistent to 6-hydroxydopamine and reserpine were the manifestations of affective aggressive behavior caused by muscarine. The autonomic phenomena were of mild intensity. It is concluded that intact central catecholamine and 5-hydroxytryptamine networks are required for expression of emotional behavior, especially vocalization (hissing and snarling), in affective type aggression. However, intact central catecholamine and 5-hydroxytryptamine pathways are not needed for the performance of attack and biting behavior 24 references. (Author abstract modified)

004174 Bellarosa, Audrey; Bedford, John A.; Wilson, Marvin C. Wilson: Dept. of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Sociopharmacology of d-amphetamine in Macaca arctoides.** Pharmacology Biochemistry and Behavior. 13(2):221-228, 1980.

The social behavior of a heterosexual group of adult monkeys (Macaca arctoides) was examined after d-amphetamine was administered to a single member or to all members of the group. Low doses of d-amphetamine increased vocalization, self-grooming, playing, social grooming, and aggression. High doses decreased most forms of social interaction. All doses increased presenting behavior. Mounting increased only when all Ss were dosed. 28 references. (Author abstract modified)

004175 Bentall, A. C. C.; Herberg, L. J. Herberg: Experimental Psychology Laboratory, Institute of Neurology, Queen Square, London WC1N 3BG, England **Blockade of amphetamine-induced locomotor activity and stereotypy in rats by spiroperidol but not by an atypical neuroleptic, thioridazine.** Neuropharmacology. 19(8):699-703, 1980.

Spiroperidol (0.025 to 0.1mg/kg i.p.) a typical neuroleptic drug produced a dose-related depression of amphetamine-induced locomotion and stereotypy in male Lister rats, but the atypical antischizophrenic drug thioridazine (5.0 to 20mg.kg) had no effect on either drug-induced behavior. Since previous studies have shown that amphetamine-induced locomotion reflects mesolimbic dopaminergic activity, these findings do not support the hypothesis that thioridazine acts selectively on the mesolimbic dopamine system. The possibility that the behavioral effects of low doses of thioridazine are not mediated by dopamine receptors is discussed. 26 references. (Author abstract modified)

004176 Bernardi, M. M.; Neto, J. Palermo. Neto: Faculty of Veterinary Medicine, University of Sao Paulo, Cidade U:niversitaria, CUASO, Bloco B-4 CEP 05508, Sao Paulo, Brazil **Effects of abrupt and gradual withdrawal from long-term haloperidol treatment on open field behavior of rats.** Psychopharmacology. 65(3):247-250, 1979.

The effects of abrupt and gradual withdrawal from long-term haloperidol treatment on rat behavior were compared. Abrupt withdrawal induced a significant increase in all parameters of activity observed except defecation. This increase was higher 72 hours after the last haloperidol injection when compared to controls. Results were considered to be a consequence of supersensitivity of central dopaminergic receptors. These differences were almost unobservable in animals gradually withdrawn, thus suggesting that the phenomenon is reversible. It is emphasized that any treatment which effects one biogenic system could have consequences on the dynamic balance of the various brain neurotransmitter substances. 15 references. (Author abstract modified)

004177 Bernet, F.; Denimal, J. Universite des Sciences at Techniques de Lille, B. P. 36, F-59650, Villeneuve d'Ascq, France / **Emotional reactivity and neurovegetative balance in the rat./** Reactivite emotionelle at equilibre neurovegetatif chez le rat. Psychopharmacology. 61(2):191-195, 1979.

The hypothesis that emotional reactivity in rat strains is related to physiological differences in a certain neurovegetative balance was investigated in 12 male Wistar and 12 male Sprague-Dawley rats by means of differential blockade of the autonomic nervous system by atropine and propranolol. The heartrate response of the emotionally reactive strain to propranolol was statistically smaller than that of the nonreactive strain, although the heartrate increase resulting from atropine treatment was more elevated in the reactive strain. The calculated sympathetic and parasympathetic tones were 8% and 30%, respectively, in the reactive rats. However, both of the tones were 14% in the nonreactive rats. It is concluded that high defecating rats in open-field trials exhibit a lower sympathetic tone linked with a higher parasympathetic tone. 4 references. (Journal abstract modified)

004178 Bhattacharyya, A. K.; Ghosh, B.; Aulakh, C. S.; Pradhan, S. N. Dept. of Pharmacology, Howard University College of Medicine, Washington, DC **Correlation of behavioral and neurochemical effects of acute administration of methylphenidate in rats.** Progress in Neuro-Psychopharmacology. 4(2):129-136, 1980.

The relationship between behavioral and neurochemical effects of acute administration of methylphenidate was investigated in rats. Methylphenidate was found to increase spontaneous motor activity and to produce stereotyped behavior at 5 to 20mg/kg ip. With the increase of dose, the total count as well as the peak level of spontaneous motor activity during the 3 hr sessions decreased, but those for stereotyped behavior increased. Neurochemically, levels of norepinephrine (NE and serotonin (5-HT) in pons/medulla and diencephalon/midbrain decreased significantly, while dopamine in caudate nucleus and diencephalon/midbrain increased significantly at 30 and 60 min following injection of 10mg/kg of methylphenidate. 34 references. (Author abstract modified)

004179 Bodnar, Richard J.; Kelly, Dennis D.; Brutus, Martin; Greenman, Carol B.; Glusman, Murray. Dept. of Behavioral Physiology, NYS Psychiatric Institute, New York, NY 10032 **Reversal of stress-induced analgesia by apomorphine, but not by amphetamine.** Pharmacology Biochemistry and Behavior. 13(2):171-175, 1980.

The effects of d-amphetamine (0.25, 0.5, 1, and 2mg/kg i.p.) and apomorphine (0.025, 0.05, 0.1, and 0.2mg/kg i.p.) on stress-

induced analgesia were studied in male Sprague-Dawley rats. No dose of amphetamine or apomorphine alone altered pain thresholds in an operant liminal escape procedure. The two low doses of amphetamine slightly potentiated the analgesia induced by 2-deoxy-D-glucose (2-DG), but amphetamine did not affect analgesia induced by cold water swims (CWS). The 0.05 and 0.1mg/kg doses of apomorphine reversed the analgesia induced by CWS or 2-DG. Results suggest that brain catecholamines are involved in stress-induced analgesia. 55 references. (Author abstract modified)

004180 Brandao, M. L.; Fontes, J. C. S.; Graeff, F. G. Dept. of Pharmacology, School of Medicine, 14.100 Ribeirao Preto, S.P., Brazil **Facilitatory effect of ketamine on punished behavior.** Pharmacology Biochemistry and Behavior. 13(1):1-4, 1980.

The effects of ketamine, pentobarbital, and amphetamine on punished and unpunished responding were studied in pigeons trained to perform under a multiple fixed-interval (FI) 5 minute, FI 5 minute schedule of food presentation. Low doses of ketamine (1.7 to 5.6mg/kg) caused moderate increases in punished FI responding without signficantly altering unpunished reponse rates, but larger doses (10 and 17mg/kg) decreased punished and unpunished FI responding. A 10mg dose of pentobarbital caused large increases in punished responding; a 17mg/kg dose of pentobarbital decreased unpunished FI response rates, but increases in punished responding without altering unpunished responding in doses of 0.17 to 1.0mg/kg, but higher does also decreased unpunished FI rates to some degree. 27 references. (Author abstract modified)

004181 Braveman, Norman S. Dept. of Psychology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada **The role of blocking and compensatory conditioning in the treatment preexposure effect.** Psychopharmacology. 61(2):177-189, 1979.

The role of blocking and compensatory conditioning in the treatment preexposure effect was investigated. Rats were given injections of an aversion inducing drug in one environment, and then conditioned to avoid a novel tasting saccharin solution. The treatment preexposure effect (i.e., reduced conditioning) was obtained when preexposure and aversion training took place in the same environment, but not in different environments. Additional experiments, which show that consumption of a novel sacharin solution is selectively enhanced, rat has than reduced, following exposure to aversion inducing drugs, give evidence that interference in the formation of conditioned taste aversions is not the result of associative blocking. Results of the final experiment suggest that enhanced drinking may have occurred because stimuli that characterized the environment in which preexposures were administered suppress the action of the pituitary/adrenal system. 30 references. (Author abstract modified)

004182 Brown, Janet; Handley, Sheila L. Pharmacological Laboratories, Dept. of Pharmacy, University of Aston, Gosta Green, Birmingham B4 7ET, England **The development of catalepsy in drug-free mice on repeated testing.** Neuropharmacology. 19(7):675-678, 1980.

Only 1.21% of male TO mice retained an imposed posture for more than 5 seconds on the first trial of a multiple trial catalepsy test, but 24% showed catalepsy on the eighth trial. In this 24%, median posture retention time increased from 0 to 12 seconds with repeated testing. Postural retention in these animals resembled haloperidol-induced catalepsy and was reduced by atropine and apomorphine but not naloxone. 11 references. (Author abstract modified)

004183 Browne, R. G.; Segal, D. S. Pharmacology Dept., Pfizer Inc., Groton, CT 06340 **Alterations in beta-endorphin-induced locomotor activity in morphine-tolerant rats.** Neuropharmacology. 19(7):619-621, 1980.

Locomotor activity was studied in male Wistar rats given morphine or beta-endorphin after pretreatment for 9 days with saline or morphine. The morphine pretreatment caused qualitatively similar alterations in the biphasic response patterns to morphine and beta-endorphin. Results suggest that the same mechanisms subserve the behavioral effects produced by opiates and opioid peptides. 10 references. (Author abstract modified)

004184 Buckett, W. R. Centre de Recherche Merrell International, 16, rue d'Ankara, F-67084 Strasbourg Cedex, France **Irreversible inhibitors of GABA transaminase induce antinociceptive effects and potentiate morphine.** Neuropharmacology. 19(8):715-722, 1980.

The GABA transaminase inhibitors gamma-acetylenic GABA and gamma-vinyl GABA had antinociceptive effects in the hot-plate test in female CD1 mice and in a tail stimulation procedure in male Sprague-Dawley rats. The antinociceptive effects were antagonized by a subconvulsive dose of bicuculline in rats, but were not blocked by naloxone in mice. Gamma-acetylenic GABA and gamma-vinyl GABA both enhanced the analgesic actions of morphine in mice, but failed to alter the naloxone precipitated morphine withdrawal syndrome in rats. The antinociceptive effects of the GABA transaminase inhibitors were related to increased brain GABA levels and did not appear to involve opioids. 30 references. (Author abstract modified)

004185 Burgess, J. Wesley; Witt, Peter N.; Phoebus, Eric; Weisbard, Charles. Dept. of Psychology, University of California, Davis CA 95616 **The spacing of rhesus monkey troops changes when a few group members receive delta9-THC or d-amphetamine.** Pharmacology Biochemistry and Behavior. 13(1):121-124, 1980.

D-amphetamine (2mg/kg) or delta9-tetrahydrocannabinol (THC, 4mg/kg) was given to a few high ranking monkeys in free ranging troops of 18-25 rhesus macaques housed in large enclosures. When three or four animals were drugged, the entire group moved closer together and group spacing was more variable. Acute changes were seen during the first week of THC and after THC was withdrawn. Chronic behavioral changes were observed after both drugs. 17 references. (Author abstract modified)

004186 Campbell, Alexander; Herschel, Michael; Cohen, Bruce M.; Baldessarini, Ross J. Dept. of Psychiatry, Harvard Medical School, Belmont, MA 02178 **Tissue levels of haloperidol by radioreceptor assay and behavioral effects of haloperidol in the rat.** Life Sciences. 27(8):633-640, 1980.

A radioreceptor assay verified by independent biochemical methods was used to evaluate tissue levels of neuroleptic activity in serum and brain extracts after injections of haloperidol in the rat. The assay detected activity between doses of 0.1 and 10mg/kg at times between 0.25 and 12 hours. Tissue levels in blood and brain were highly correlated and corresponded well with a behavioral test of catalepsy at 1 hour after drug administration. This relationship between brain levels and behavior persisted but changed quantitatively over time. 12 references. (Author abstract)

004187 Cananzi, A. R.; Costa, E.; Guidotti, A. Costa: Lab. of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Potentiation by intraventricular muscimol of the anticonflict effect of benzodiazepines.** Brain Research. 196(2):447-453, 1980.

The anticonflict action of muscimol (a potent GABA receptor agonist) and its ability to potentiate the anticonflict action of the benzodiazepines were studied in rats using Vogel's procedure. Rats were injected intraventricularly with a dose of muscimol from 50 to 200ng to study whether the anticonflict action is dose related. The potency of a 200ng dose of muscimol is comparable to the potency of an anticonflict dose of 0.5mg i.v. of diazepam. 4,5,6,7-Tetrahydroisoxaxolo-(5,4-c)pyridin 3-ol (THIP), a muscimol analogue with weaker intrinsic GABA mimetic activity, is active in doses 10 times higher than muscimol. The threshold dose of diazepam to elicit anticonflict action was markedly potentiated when it was injected 5 min after intraventricular muscimol. These data support the concept that GABA receptors may be involved in the anticonflict effects of the benzodiazepines. 22 references. (Author abstract modified)

004188 Carey, Robert J. State University of New York, Upstate Medical Center, Syracuse, NY 13210 **Facilitation of responding for rewarding brain stimulation by a high dose of amphetamine when hyperthermia is prevented.** Psychopharmacology. 61(3):267-271, 1979.

The role of hyperthermia in the facilitation of responding for rewarding brain stimulation by high dose amphetamine was investigated. Rats given a 5mg/kg injection of d-amphetamine did not respond for brain stimulation reward when tested under normal laboratory temperatures. In addition to the usual manifestations of stereotypy, the rats were markedly hyperthermic. If the hyperthermia was prevented, however, by initially placing the rats in a cold room (10 degrees C) and subsequently testing for brain stimulation under a cool chamber temperature (14 to 16 degrees C), the rats responding for brain stimulation was facilitated. Thus, the occurrence of hyperthermia appears to be a critical factor responsible for this behavioral dysfunction produced by a high dose of amphetamine. 22 references. (Author abstract modified)

004189 Castellano, Claudio. Laboratorio di Psicobiologia e Psicofarmacologia del C. N. R., Via Reno 1, I-00198 Rome, Italy **Effects of LSD-25 on avoidance behavior and locomotor activity in mice.** Psychopharmacology. 62(2):145-149, 1979.

Avoidance behavior and locomotor activity were investigated in C57BL/6 (C57) mice who were tested in a shuttle box under the influence of LSD-25 in two sets of experiments. In the first set, the pretrial administrations of LSD (0.05, 0.1, and 0.2mg/kg) were followed by dose related performance improvements. In the second set, the posttrial administration of LSD(0.2mg/kg) immediately after each experimental session improved the performances of the mice. No effect was evident when the hallucinogen was injected 2 h after training, thus showing that LSD improved the memory processes of the C57 mice in these experimental conditions. Dose related activity depressant effects were evident in a third set of experiments, carried out in a toggle floor box. 41 references. (Author abstract)

004190 Caza, Patricia A.; Spear, Linda Patia. Spear: Dept. of Psychology, SUNY, Binghamton, NY 13901 **Ontogenesis of morphine-induced behavior in the rat.** Pharmacology Biochemistry and Behavior. 13(1):45-50, 1980.

Behavioral responses to morphine sulfate (o.1, 0.5, 1.0, and 5.0mg/kg i.p.) were studied in 10, 17, and 24-day-old Sprague-Dawley rats. At 10 days of age, the predominant response to morphine was depression of locomotor activity; the lowest dose had no effect, and the highest dose-induced catalepsy. On postnatal day 17, a 0.5mg/kg dose of morphine increased locomotion, but a 5mg/kg dose depressed locomotion and induced catalepsy. Stereotypic gnawing was observed in 24-day-old rats treated with 5mg/kg morphine, but no does significanly altered activity at this age. 21 references. (Author abstract modified)

004191 Celedon, J. M.; Colombo, M. Instituto de Nutricion y Tecnologia de los Alimentos, Universidad de Chile, P.O. Box 15 138, Santiago 11, Chile **Effects of chlordiazepoxide on maze performance of rats subjected to undernutrition in early life.** Psychopharmacology. 63(1):29-32, 1979.

Isolated effects of undernutrition and emotional reactivity on maze performance in rats were studied comparing the effects of chlordiazepoxide on learing performance in an undernourished group of adult rats and on a control group. Chlordiazepoxide improved performance in the early undernourished group but impaired the performance of the normal group. This supports the hypothesis that the high emotional level of previously undernourished subjects acts negatively upon problem-solving performance. 30 references. (Author abstract modified)

004192 Chadwick, D.; Jenner, P.; Marsden, C. D. University Dept. of Neurology, Institute of Psychiatry, London SE5 8AF, England **5-Hydroxytryptamine and myoclonus induced by 1,2-dihydroxybenzene (catechol) in the guinea-pig.** British Journal of Pharmacology. 66(3):358-360, 1979.

Myoclonus induced by 1,2-dihydroxybenzene (catechol) in the guinea-pig was not altered by pharmacological manipulation of cerebral 5-hydroxytryptamine (5-HT) with quipazine, 5-hydroxytryptophan, cyproheptadine, methergoline, or p-chlorophenylalanine. Clonazepam, which effectively controls 5-HT dependent postanoxic action myoclonus in humans, also failed to alter the catechol-induced myoclonus in guinea-pigs. No significant alterations in 5-HT or 5-hydroxyindoleacetic acid levels were found in brain regions of animals killed during the catechol-induced myoclonus. Results-indicate that catechol induced myoclonus is not associated with changes in cerebral 5-HT function and therefore not relevant to postanoxic action myoclonus in humans. 13 references. (Author abstract modified)

004193 Chance, William T. Dept. of Surgery, University of Cincinnati Medical Center, Cincinnati, OH 45267 **Autoanalgesia: opiate and non-opiate mechanisms.** Neuroscience and Biobehavioral Reviews. 4(1):55-67, 1980.

Autoanalgesia (behaviorally activated antinociception) was elicited by lesion-induced hyperemotionality or by classical conditioning of fear in rats. Hyperemotionality and antinociception showed parallel declines with daily handling in rats with septal lesions and after diazepam treatment in rats with lesions of the ventromedial hypothalamus. Autoanalgesia elicited by conditioned fear was blocked by spinal cord transection, but not by diazepam. Opiate binding experiments suggested the involvement of endorphins in the autoanalgesia, but hypophysectomy, morphine tolerance, and very high doses of opiate antagonists all failed to reduce the antinociception. Autoanalgesia was significantly reduced by electrolytic lesions of the nucleus raphe magnus, a descending serotonergic system. 65 references. (Author abstract modified)

004194 Clemens, Lynwood G.; Dohanich, Gary P. Hormones and Behavior Lab, Biology Research Center, Michigan State University, East Lansing, MI 48824 **Inhibition of lordotic behavior in female rats following intracerebral infusion of anticholinergic agents.** Pharmacology Biochemistry and Behavior. 13(1):89-95, 1980.

Cholinergic antagonists were bilaterally infused into forebrain areas of overiectomized female Sherman rats treated with estrogen and progesterone. Infusion of the acetylcholine (ACh) synthesis inhibitor hemicholinium-3 decreased the incidence of lordotic behavior, and this inhibition was prevented by simulta-

neous infusion of choline chloride. Atropine sulfate, an ACh receptor blocker, also reduced lordotic behavior. Results suggest that lordosis is facilitated by central cholinergic activity. 34 references. (Author abstract modified)

004195 Clemens, Lynwood G.; Humphrys, Raymond R.; Dohanich, Gary P. Hormones and Behavior Lab, Biology Research Center, Michigan State University, East Lansing, MI 48824 **Cholinergic brain mechanisms and the hormonal regulation of female sexual behavior in the rat.** Pharmacology Biochemistry and Behavior. 13(1):81-88, 1980.

Cholinergic muscarinic stimulation of the medial preoptic area of the mesencephalic reticular formation with carbachol or bethanechol facilitated lordosis in ovariectomized female Sherman rats treated with estrogen. Adrenalectomy did not abolish the facilitative influence of cholinergic stimulation in the preoptic areas. Implants of carbachol in the neocortex did not influence lordosis. 39 references. (Author abstract modified)

004196 Clody, Donald E.; Carlton, Peter L. CNS Biology, Lederle Laboratories, Pearl River, NY 10965 **Stimulus efficacy, chlorpromazine, and schizophrenia.** Psychopharmacology. 69(2):127-131, 1980.

The effects of chlorpromazine (CPZ) on rat discrimination learning were studied in a variation of Migler's (1975) procedure, and the role of stimulus efficacy in the neuroleptic management of schizophrenic symptoms is discussed. In the experimental procedure, the stimulus efficacy was varied in terms of both proximity to reinforcement and amount of reinforcement. The behavioral effects of CPZ were found to be significantly modulated by stimulus efficacy and increases in efficacy attenuated drug effect. The relevance of this finding to various conjectures about the deficits seen in schizophrenia is discussed. 12 references. (Author abstract modified)

004197 Collins, Robert C. Dept. of Neurology, St. Louis City Hospital, 1515 Lafayette, St. Louis, MO 63104 **Anticonvulsant effects of muscimol.** Neurology. 30(6):575-581, 1980.

Systemic injection of the GABA agonist muscimol (7mcmol/kg) blocked topical penicillin seizures and delayed the onset of generalization metrazol convulsion in Sprague-Dawley rats. Higher doses of muscimol caused bradykinesia, ataxia, catatonic posturing, and slowing of the EEG. When applied topically to cortex, muscimol blocked focal penicillin, bicuculline, and picrotoxin discharges in a dose dependent manner but had no effect against strychnine. (Author abstract modified)

004198 Colpaert, F. C.; Niemegeers, C. J. E.; Janssen, P. A. J. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Factors regulating drug cue sensitivity: the effect of training dose in fentanyl-saline discrimination.** Neuropharmacology. 19(8):705-713, 1980.

Male Wistar rats were trained to discriminate fentanyl from saline at training doses of 0.025, 0.005, 0.01, 0.02, and 0.04mg/kg. Dose related effects were observed in subsequent tests of stimulus generalization from fentanyl to morphine; cyclazocine and d-amphetamine generalization to fentanyl; and naloxone antagonism of the fentanyl cue. Results suggested that fentanyl training doses of 0.02mg/kg or greater produce a discriminative stimulus complex specific for narcotic drugs, while lower doses have less pharmacological specificity. 12 references. (Author abstract modified)

004199 Cooper, S. J. Dept. of Psychology, University of Birmingham, Birmingham, B15 2TT, England **Effects of enantiomers of oxazepam sodium hemisuccinate on water intake and antagonism of picrotoxin- or naloxone-induced suppression of drinking by chlordiazepoxide in the rat.** Neuropharmacology. 19(9):861-865, 1980.

The ()-enantiomer of oxazepam sodium hemisuccinate (0.25 to 10.0mg/kg) enhanced water consumption in water deprived male black hooded rats, but the (-)-enantiomer had no significant effect. Nalozone and picrotoxin both suppressed drinking, and these effects were reversed by chlordiazepoxide. Results indicate that benzodiazepines exert a stereoselective facilitatory effect on drinking, which is antagonized by naloxone. 21 references. (Author abstract modified)

004200 Cooper, Steven J.; Francis, Raymond L. Laboratory of Experimental Psychology, University of Sussex, Falmer, Brighton, BN1 9QG, England **Feeding parameters with two food textures after chlordiazepoxide administration, alone or in combination with d-amphetamine or fenfluramine.** Psychopharmacology. 62(3):253-259, 1979.

The influence of food texture on feeding performance after chlordiazepoxide administration, alone or in combination with amphetamine or fenfluramine, was examined in rats. Chlordiazepoxide reduced the rate of eating and extended the duration of feeding in a 10 minute feeding test. Fenfluramine reduced eating rate without affecting eating duration, while amphetamine reduced eating duration without reducing eating rate. Food texture affected feeding behavior; rats ate standard diet in pellet form faster than powdered food, although they spent longer eating the powdered food. Textural differences did not significantly interact with the changes in feeding responses induced by the three drugs, except that latency to eat after either amphetamine or fenfluramine injection, when pellets were available, was significantly prolonged. It is concluded that characterizing drug effects on feeding in terms of a two dimensional matrix of eating rate and duration is recommended, rather than relying solely on amount of food consumption as the measure of drug effects. 17 references. (Author abstract modified)

004201 Costain, D. W.; Green, A. R.; Grahame-Smith, D. G. University Dept. of Clinical Pharmacology, Radcliffe Infirmary, Oxford, England **Enhanced 5-hydroxytryptamine-mediated behavioural responses in rats following repeated electroconvulsive shock: relevance to the mechanisms of the antidepressive effect of electroconvulsive therapy.** Psychopharmacology. 61(2):167-170, 1979.

The enhanced 5-hydroxytryptamine (5-HT) mediated behavioral responses in rats following repeated electroconvulsive shock (ECS) are described, and its relevance to the mechanism of the antidepressant effect of electroconvulsive therapy (ECT) is discussed. Treatment of rats with one ECS per day for 10 dyas enhanced the hyperactivity syndrome produced by administration of tranylcypromine and L-tryptophan given 24 hours after the final shock. Similar enhancement was seen whether the shock was alternating sinusoidal or direct current (fractionated), whether it was given through unilaterally or bilaterally placed electrodes and whether or not a neuromuscular blocking agent (fazadinium) was used. Five shocks spread over 10 days or eight shocks spread over 17 days were similarly effective, while eight shocks in 1 day were ineffective. Therefore, when ECS are given to rats in ways similar to those in which ECT is gieven to human subjects with depression, enhancement of behavioral responses to increased 5-HT function is produced. 18 references. (Author abstract modified)

004202 Costall, B.; De Souza, C. X.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, BD7 1DP, England **Topographical analysis of the actions of 2-(N,N-dipropyl)amino-5,6-dihydroxytetralin to cause**

biting behaviour and locomotor hyperactivity from the striatum of the guinea-pig. Neuropharmacology. 19(7):623-631, 1980.

Male Dunkin-Hartley guinea-pigs were examined for locomotor hyperactivity and biting behavior after injection of the dopamine agonist 2-(N,N-dipropyl)amino-5,6-dihydroxytetralin at 78 locations within and around the striatum. Results revealed a differential distribution of sites involved in the two behaviors. In general, hyperactivity was most marked after injections in lateral regions, particularly their dorsal portions, whereas biting was most marked after injections in the ventromedial caudate. The drug-induced hyperactivity was antagonized by the neuroleptics fluphenazine and tiapride but not by atropine, methysergide, dl-propranolol, or piperoxan. 16 references. (Author abstract modified)

004203 Cowen, P. J.; Nutt, D. J.; Green, A. R. MRC Unit, Dept. of Clinical Pharmacology, Radcliffe Infirmary, Oxford, OX2 6HE, England **Enhanced 5-hydroxytryptamine and dopamine-mediated behavioural responses following convulsions -- II. The effects of anaesthesia and current conditions on the appearance of enhanced responses following electroconvulsive shock.** Neuropharmacology. 19(9):901-906, 1980.

The effects of electroconvulsive shock (ECS) on behavioral responses mediated by dopamine and 5-hydroxytryptamine were examined in male Sprague-Dawley rats. Fewer ECSs were required to enhance behavioral responses to tranylcypromine (TCP) and L-DOPA than to enhance responses to TCP and L-tryptophan. Halothane and methohexitone both retarded the appearance of the enhanced response to TCP and L-DOPA, and those changes were not due to the anesthetics$? effect on the severity of convulsions. Changes in seizure duration or voltage passed did not affect the enhancement of behavior after ECS. 20 references. (Author abstract modified)

004204 Crawley, Jacqueline; Goodwin, Frederick K. Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bldg. 10, Rm. 4S239, Bethesda, MD 20205 **Preliminary report of a simple animal behavior model for the anxiolytic effects of benzodiazepines.** Pharmacology Biochemistry and Behavior. 13(2):167-170, 1980.

Clonazepam and chlordiazepoxide produced dose dependent facilitation of exploratory behavior in male albino mice allowed to move freely between a dark enclosure and a larger lighted open-field. This increase does not reflect a nonspecific increase in general motor activity, since the benzodiazepines did not significantly alter locomotion in mice tested in a bare, undifferentiated cage. Results suggest that this model of exploratory behavior may be useful in studies of the anxiolytic effects of benzodiazepines. 23 references. (Author abstract modified)

004205 Cutler, Margaret G.; Moore, Michael R.; Ewart, Franzeska G. Dept. of Biological Sciences, Glasgow College of Technology, Cowcaddens Road, Glasgow, G4 OBA, Scotland **Effects of delta-aminolaevulinic acid administration on social behaviour in the laboratory mouse.** Psychopharmacology. 61(2):131-135, 1979.

The effects of delta-aminolaevulinic acid (ALA) on unrestrained social behavior were examined using ethologic analysis of social encounters between mice. After a dose level of 1.6mmol ALA/kg, male and female mice showed periods of immobility and scanned less frequently than saline injected control Ss. Exploration of the cage was significantly reduced in frequency in treated males, many elements of social and sexual investigation were reduced in treated females, and no elements of aggression were seen in treated males. Gait was abnormal and movement lethargic in animals showing the greatest degree of immobility. Righting reflexes and the response to stimuli of noise and touch remained normal. After a dose level of 0.8mmol ALA/kg, no significant behavioral effects were detectable. 33 references. (Author abstract modified)

004206 Cytryn, Albert S. 10301 Georgia Avenue, Apartment 101, Silver Spring, MD 20901 **The effect of varying doses of d-amphetamine on activity levels of prepubertal mice.** Psychiatry Research. 3(1):41-51, 1980.

The effect of varying doses of d-amphetamine on the activity level of C57BL/6J mice, DBA/1J, C3H/HeJ, and C3D2F1 prepubertal mice (25 to 30 days old) was investigated. Activity was measured by the use of an activity cage with a revolving drum. After determination of baseline activity level, the animals were assigned to the following set of intraperitoneal injections: normal saline; or d-amphetamine .2,.5, or 5mg/kg. The mean activity level of the C57BL/6J mice was significantly higher than that of the other strains. The mean activity level after 5mg/kg d-amphetamine was significantly lower than after other dosages in all strains. All strains responded similarly to d-amphetamine as is apparent from the parallel profiles for the dose/response curves. The response of d-amphetamine is at variance with the known response of mature mice. Results are discussed with reference to the paradoxical response to d-amphetamine and its use in ameliorating behavioral and learning problems in hyperactive children. 67 references. (Author abstract modified)

004207 Czech, Donald A.; Stein, Elliot A. Dept. of Psychology, Marquette University, 617 N. 13th Street, Milwaukee, WI 53233 **Naloxone depresses osmoregulatory drinking in rats.** Pharmacology Biochemistry and Behavior. 12(6):987-989, 1980.

The effect of the opiate antagonist naloxone on hypertonic CaCl-induced drinking was studied in rats in a within S design. Naloxone reduced drinking at all dosage levels used (0.3 to 10.0mg/kg) when compared to a control condition. These results extend previous findings of naloxone mediated reduction in fluid intake in water deprived and osmotically challenged animals. Naloxone's effect on fluid intake seems to be independent of procedure employed, and thus, quite general. Possible mechanisms are discussed. 15 references. (Author abstract)

004208 Davis, Kenneth L.; Kastin, Abba J.; Beilstein, Barbara A.; Vento, Adela L. Dept. of Psychiatry, Bronx Veterans Administration Medical Center, Bronx, NY 10468 **MSH and MIF-I in animal models of tardive dyskinesia.** Pharmacology Biochemistry and Behavior. 13(1):37-40, 1980.

The effects of alpha-melanocyte stimulalting hormone (MSH) and MSH release inhibiting factor (MIF-I) were studied in an animal model of tardive dyskinesia. In male Sprague-Dawley rats chronically pretreated with haloperidol to augment responses to dopamine agonists, MSH and MIF-1 increased the stereotype induced by 0.125mg/kg apomorphine. This finding suggests that MSH and MIF-1 may weakly increase dopaminergic transmission. 36 references. (Author abstract modified)

004209 Davis, Michael. Connecticut Mental Health Center, 34 Park St., New Haven, CT 06508 **Neurochemical modulation of sensory-motor reactivity: acoustic and tactile startle reflexes.** Neuroscience and Biobehavioral Reviews. 4(2):241-263, 1980.

The use of the startle reflex as a model system for evaluating drug effects on stimulus reactivity and reflex excitability is discussed. The modulation of the startle reflex by serotonin, dopamine, norepinephrine, acetylcholine, and opiates is reviewed. The effects of prior associative learning on habituation, sensitization, and potentiation of startle are also considered. 187 references. (Author abstract modified)

004210 De Caro, G.; Mariotti, M.; Massi, M.; Micossi, L. G. Institute of Pharmacology, University of Camerino, Via Scalzino 5, I-62032 Camerino, Italy **Dipsogenic effect of angiotensin II, bombesin and tachykinins in the duck.** Pharmacology Biochemistry and Behavior. 13(2):229-233, 1980.

Intracerebroventricular injections of angiotensin-II, bombesin, and eledoisin elicitited dose dependent dipsogenic effects in ducks. Substance-P had no marked effect. It is suggested that bombesin and tachykins stimulate water intake in birds, but inhibit drinking in mammals. 16 references. (Author abstract modified)

004211 de Caro, G.; Massi, M.; Micossi, L. G. Institute of Pharmacology, University of Camerino, I-62032 Camerino, Italy **Bombesin potently stimulates water intake in the pigeon.** Neuropharmacology. 19(9):867-870, 1980.

Intracerebroventricular injections of bombesin evoked a potent, dose dependent dipsogenic response in the pigeon. No other behavioral alterations were observed. Results suggest that endogenous bombesin or related peptides may be involved in the control of water intake in the pigeon. 17 references. (Author abstract modified)

004212 De Lima, T. C. M.; Neto, J. Palermo. Neto: Laboratory of Therapeutics, Cuaso, Bloco B/4, CEP 05508 Sao Paulo, Brazil **The effects of diphenylhydantoin on rat behavior.** Psychopharmacology. 69(2):183-185, 1980.

The effects of abrupt withdrawal from long-term diphenylhydantoin (DPH) treatment or openfield behavior of rats were investigated. Since the extrapyramidal syndrome induced in grand-mal and focal epilepsy patients by DPH resembles those produced by neuroleptic drugs, such as haloperidol, which are suspected of blocking dopamine (DA) receptors, the possible interference of DPH with the stereotyped behavior induced by apmorphine (AP) treatment was examined. Animals were administered increasing doses of DPH for 20 days, and were observed in the open-field during withdrawal. Results suggest that chronic DPH administration leads to a central supersensitivity phenomenon. Possible interference of DPH with dopaminergic systems is discussed. 11 references. (Author abstract modified)

004213 Dennis, Stephen G.; Melzack, Ronald. Neurosciences Research Program, 165 Allandale Street, Boston, MA 02130 **Pain modulation by 5-hydroxytryptaminergic agents and morphine as measured by three pain tests.** Experimental Neurology. 69(2):260-270, 1980.

The effects on pain and morphine analgesia of drugs affecting 5-hydroxytryptaminergic (5-HT) function were assessed using three pain tests in rats. Each behavioral test (tail flick, hotplate, and formalin) yielded a unique constellation of tryptaminergic influences. The salient drug effects included: 1) analgesia produced by L-tryptophan in the tail flick and formalin tests but not in the hotplate test; 2) dose dependent, biphasic facilitatory and inhibitory effects on morphine analgesia of p-chlorophenylalanine and p-chloroamphetamine in the formalin test; and 3) facilitation of morphine analgesia by methysergide and L-tryptophan in the formalin test. Data suggest that differences in the type of noxious stimulation and in the motor responses required in various pain tests are crucial in determining the observed pharmacologic profile of pain and opiate analgesia. 53 references. (Author abstract)

004214 Dohanich, Gary P.; Ward, Ingeborg L. Ward: Dept. of Psychology, Villanova University, Villanova, PA 19085 **Sexual behavior in male rats following intracerebral estrogen application.** Journal of Comparative and Physiological Psychology. 94(4):634-640, 1980.

The effects on sexual behavior and morphology of estradiol benzoate (EB) applied directly to the medial preoptic nucleus were assessed in three groups of male rats with varying sexual behavior potentials. High levels of lordotic behavior were observed in all EB treated groups. Cholesterol was uniformly ineffective. Central EB failed to facilitate male copulatory behavior in any group. However, there was evidence that cannula implantation may have impaired the potential for male behavior. Significant reductions in testis and epididymis weights were evident in some but not all EB treated males. It is concluded that EB can activate lordotic behavior consistently in male rats if applied in sufficient amounts to the medial preoptic region. 23 references. (Author abstract)

004215 Duncan, Charles; Deitrich, Richard A. Dept. of Pharmacology, University of Colorado, 4200 E. 9th Ave., Denver, CO 80262 **A critical evaluation of tetrahydroisoquinoline-induced ethanol preference in rats.** Pharmacology Biochemistry and Behavior. 13(2):265-281, 1980.

Infusions of tetrahydropaveroline (THP) and salsolinol resulted in increased alcohol intake in Sprague-Dawley and Long-Evans rats. This effect persisted for up to 10 months, but no signs of dependence or withdrawal were observed. Extensive dose/response studies showed THP in a daily dose of 104 nM inhibited alcohol consumption. 39 references. (Author absatract modified)

004216 Dzoljic, M. R.; Poel-Heisterkamp, A. L. v. d. Dept. of Pharmacology, Medical School, Erasmus University, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands. **The role of the nucleus accumbens and nigrostriatum in enkephalin-induced myoclonus.** Pharmacology Biochemistry and Behavior. 13(1):103-106, 1980.

Local administration of the enkephalin analog D-Ala2-Met5-enkephalinamide (DALA) into the nucleus accumbens or caudate nucleus of male Wistar rats resulted in myoclonic contractions (MC) of the submandibular muscles and epileptic discharges in the electrocorticogram. These pheonomena were blocked by naloxone but not by haloperidol. DALA did not induce MC when applied to the substantia nigra compacta. Results suggests that endogeneous opiates in the nucleus accumbens and striatum may be involved in the pathogenesis of some types of myoclonus. 24 references. (Author abstract modified)

004217 Egan, Josephine; Earley, Christopher J.; Leonard, B. E. Leonard: Pharmacology Dept., University College, Galway, Ireland **The effect of amitriptyline and mianserine (Org. GB94) on food motivated behaviour of rats trained in a runway: possible correlation with biogenic amine concentration in the limbic system.** Psychopharmacology. 61(2):143-147, 1979.

The effect of amitriptyline and mianserine (ORG. GB94) on food motivated behavior of rats trained in a runway is described, and possible correlations of this effect with biogenic amine concentration in the limbic system are discussed. Rats on a 23 hour food deprivation schedule were trained to run down a straight runway for a food reward. Neither amitriptyline nor mianserine had an effect on the running time for the food reward during the period of continuous reinforcement. However, both antidepressants delayed the extinction of this response. It is judged unlikely that this effect on extinction is due to an altered motivation for the food reward, as amitriptyline significantly decreased the food intake of the experimental animals while mianserine increased the food intake throughout the period of the experiment. The observation that both these antidepressants reduce the speed of extinction of rewarded behavior may be explicable in terms of observed changes in the concen-

tration of biogenic amines in the limbic system. 22 references. (Author abstract modified)

004218 Einon, Dorothy F.; Sahakian, Barbara J. Psychological Dept., Durham University, Science Laboratories, South Road, Durham-DH1 3LE, England **Environmentally-induced differences in susceptibility of rats to CNS stimulants and CNS depressants: evidence against a unitary explanation.** Psychopharmacology. 61(3):299-307, 1979.

The hypothesis that socially isolated rats are more aroused than rats raised in social groups was tested by examining amphetamine-induced activity and stereotypy in social and isolated rats of both sexes in both the active and inactive phases of their diurnal activity cycle. In socially raised rats, it is possible to produce behavioral profiles similar to those of isolated rats by increasing the arousal level of the social rat. However, the complex interaction of housing conditions, diurnal variation, and gender with drug dose suggests that one intervening variable such as arousal is too simplistic an explanation. In subsequent experiments, stereotypy was enhanced by a familiar environment, and there was a clear dissociation between the effects of CNS stimulants and CNS depressants. The increased susceptibility of isolates to CNS stimulant depends on social isolation for a short period before 45 days of age; the decreased susceptibility of isolates to CNS depressants may be produced by isolation at any age. It is concluded that there is no evidence that isolated rats are hyperaroused. 36 references. (Author abstract modified)

004219 Ercan, Z. Sevim; Ilhan, Mustafa; Turker, R. Kazim. Turker: A.U. Tip Fakultesi, Farmakoloji Enstitusu, Sihhiye, Ankara, Turkey **Alterations by captopril of pain reactions due to thermal stimulation of the mouse foot: interactions with morphine, naloxone and aprotinin.** European Journal of Pharmacology. 63(2/3):167-177, 1980.

The angiotensin converting enzyme inhibitor captopril (0.1 to 0.4mg/kg) significantly increased reaction times of mice in a hotplate test 4 hours after subcutaneous injection, but not at other times. Captopril also increased jumping in some animals, and this effect was greater with lower doses. Morphine alone increased reaction times but not jumping. Reaction times were increased in animals treated with captopril and morphine or aprotinin. Aprotinin and morphine both blocked the jumping response to captopril. 28 references. (Author abstract modified)

004220 Esposito, Ralph U.; Perry, William; Kornetsky, Conan. Boston University School of Medicine, Laboratory of Behavioral Pharmacology, Div. of Psychiatry, 80 E. Concord St. L-602, Boston, MA 02118 **Effects of d-amphetamine and naloxone on brain stimulation reward.** Psychopharmacology. 69(2):187-191, 1980.

Self-stimulation thresholds were determined in rats by means of a modification of the psychophysical method of limits, and reinforcement values were determined after the administration of d-amphetamine alone, naloxone alone, and naloxone administered concurrently with d-amphetamine. d-Amphetamine yielded dose related decreases in the threshold, while naloxone alone caused no consistent changes. For each animal, a dose of d-amphetamine that substantially lowered the threshold was then selected to be administered with varying doses of naloxone. The threshold lowering effect of d-amphetamine was blocked by naloxone at doses as low as 2.0 or 4.0mg/kg. This finding suggests the possible involvement of an opiate receptor in the mediation of the enhancement by d-amphetamine of brain stimulation reward. 25 referencs. (Author abstract modified)

004221 Fairbairn, J. W.; Pickens, Joan T. Dept. of Pharmacognosy, School of Pharmacy, University of London, 29-39 Brunswick Square, London WC1N 1AX, England **The oral activity of delta'-tetrahydrocannabinol and its dependence on prostaglandin E2.** British Journal of Pharmacology. 67(3):379-385, 1979.

Delta'-trans-tetrahydrocannabinol (THC) induced catalepsy in male albino mice in oral doses from 0.06mg/kg upwards, with peak activity 2 to 4 hours after dosing. THC and chlorpromazine (CPZ) were equipotent as cataleptic agents during the first 2 hours after dosing, but THC activity continued to increase as CPZ activity began to decline; peak THC activity was 5.67 times greater than that of CPZ. The cataleptic effect of THC was abolished by aspirin, indomethacin, diflunisal, and phenylbutazone, which inhibit prostaglandin synthesis, and was restored by exogenous prostaglandin-E2 but not by prostaglandin-E1 or prostaglandin-F2alpha. The cataleptic effect of CPZ was not affected by pretreatment with aspirin. THC was less active after intraperitonal injection that after oral administration, and this did not appear to be due to poor absorption or extraction into fat depots. Cannabidiol showed no cataleptic effect. 25 references. (Author abstract modified)

004222 Fernando, J. C. R.; Lees, A. J.; Curzon, G. Dept. of Neurochemistry, Institute of Neurology, 33 John's Mews, London WC1N 2NS, England **Differential antagonism by neuroleptics of backward-walking and other behaviours caused by amphetamine at high dosage.** Neuropharmacology. 19(6):549-553, 1980.

The effects of some neuroleptic drugs and metoclopramide were investigated on the d-amphetamine-induced mouse behaviors of backward walking, circling, head bobbing, reciprocal forepaw treading, hind limb abduction, body shakes and Straub tail. The inhibitory effects on backward walking and circling were found to parallel each other except for alpha-flupenthixol, which was more effective against circling. Drugs which inhibited 5-hydroxytryptamine (5-HT) dependent behaviors (thioridazine), head bobbing (bromoperidol, alpha-flupenthixol) or all these behaviors (clozapine) also inhibited backward walking at the same dose, thus strengthening previous evidence that release of both 5-HT and dopamine (DA) is required for backward walking (and circling). A requirement for 5-HT is also indicated by a close relationship between the effectiveness of the drugs against backward walking and published data on their effects on tryptamine seizures. Metoclopramide, haloperidol, pimozide, and sulpiride inhibited backward walking at doses which had little effect on either other 5-HT dependent behaviors or head bobbing. The above and other relationships indicate that backward walking may be a useful animal behavioral model for studying 5-HT/DA interactions and that these may be relevant in schizophrenia. 26 references. (Author abstract modified)

004223 Figler, Michael H.; Klauenberg, B. Jon. Dept. of Psychology, Towson State University, Baltimore, MD **Pentobarbital sodium and attack behavior in male Siamese fighting fish.** Psychopharmacology. 69(2):207-208, 1980.

The effects of pentobarbital sodium on intraspecific attack behavior in male Siamese fighting fish were investigated, and results were compared with the effects of chlordiazepoxide and secobarbital sodium. Pairs of fish fought while immersed in 20micrograms/ml or 40micrograms/ml pentobarbital sodium or plain water. The 40micrograms/ml group showed significantly less attack (e.g., biting, jaw locking) than either control or low dose groups without producing a change in general arousal. Quasisexual behvior, seen in an earlier chlordiazepoxide study, did not occur in the present study. 7 references. (Author abstract modified)

004224 File, Sandra E.; Deakin, J. F. W. Dept. of Pharmacology, School of Pharmacy, University of London, 29/39 Brunswick Square, London WC1N 1AX, England **Chemical lesions of**

both dorsal and median raphe nuclei and changes in social and aggressive behaviour in rats. Pharmacology Biochemistry and Behavior. 12(6):855-859, 1980.

Lesions caused by microinjections of 5,7-dihydroxytryptamine (5,7-DHT) into both the dorsal and median raphe nuclei were found to result in 90% depletions of striatal and hippocampal 5-HT concentrations. Compared with vehicle injected controls, the lesioned rats showed reduced active social interaction scores in all four of the test conditions and also reduced levels of locomotor activity. The lesioned rats did not differ from the control Ss in their latency to start drinking in a novel environment, or in their response to intruder rats placed in their home cages, or in their behavior as intruders when they were placed in the home cages of unoperated rats. The difficulties of interpreting the behavioral effects of a lesion when the lesion produces hypoactivity, and the differences between the effects of these joint lesions of both dorsal and median raphe nuclei and the effects of separate lesions of each nucleus are discussed. 19 references. (Author abstract)

004225 Flaherty, Charles F.; Driscoll, Cynthia D. Dept. of Psychology, Busch Campus, Rutgers, The State University, New Brunswick, NJ 08903 **Amobarbital sodium reduces successive gustatory contrast.** Psychopharmacology. 69(2):161-162, 1980.

The effects of amobarital sodium (ABS) on successive negative contrast in consummatory behavior were investigated and compared with those of chlordiazepoxide (CDP). ABS produced equivalent reductions in negative contrast when injected for the first time on either day 1 or day 2 following a shift from 32% to 4% sucrose. Results imply that the mechanisms responsible for contrast on postshift days 1 and 2 are equally sensitive to a given dose of ABS, whereas earlier studies have indicated that these mechanisms are not equally sensitive to a given dose of CDP. 7 references. (Author abstract modified)

004226 Fleisher, Loyd N.; Glick, Stanley D. Institute of Psychiatric Research, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis, IN 46202 **Hallucinogen-induced rotational behavior in rats.** Psychopharmacology. 62(2):193-200, 1979.

The ability of LSD, mescaline, and 5-methoxy-N,N-dimethyltryptamine (MDMT), and some nonhallucinogenic agents that interact with serotonergic mechanisms to induce rotational behavior in normal rats was investigated. LSD, mescaline, and MDMT in normal rats induced dose dependent rotation which was consistent in direction from week to week. Of the three postsynaptic serotonin antagonists tested, only methysergide induced rotation; this rotation was consistent in direction from week to week and was in the same direction as LSD-induced rotation. The results suggest that the mechanism by which hallucinogens induce rotation is consistent with an inhibitory action on the serotonin containing midbrain raphe neurons. Methysergide-induced rotation could result from partial antagonism of postsynaptic serotonin receptors in the substantia nigra or striatum. The dopaminergic properties of LSD may attenuate rotation resulting from disinhibition of nigrostriatal activity by interacting with presynaptic nigrostriatal dopamine autoreceptors. 50 references. (Author abstract modified)

004227 Flemenbaum, Abraham. Dept. of Psychiatry, Louisiana State University Medical Center, Shreveport, LA 71130 **Failure of apomorphine to induce dopamine receptor hypersensitivity.** Psychopharmacology. 62(2):175-179, 1979.

Apomorphine, a direct dopamine agonist, is reported to have failed to induce the so called dopamine receptor supersensitivity. Furthermore, a review of the evidence strongly suggests that the mechanisms involved in this phenomenon are not purely dopaminergic. This phenomenon is more complex than one of simple changes in the sensitivity or number of a particular type of receptor. Also sexual differences were observed and the literature suggests an involvement of seortoninergic mechanisms in stereotyped behavior. 26 references. (Author abstract)

004228 Flood, James F.; Smith, Gary E.; Jarvik, Murray E. Dept. of Psychology, School of Medicine, University of California/Los Angeles, Los Angeles, CA 90024 **A comparison of the effects of localized brain administration of catecholamine and protein synthesis inhibitors on memory processing.** Brain Research. 197(1):153-165, 1980.

The effects of localized brain administration of catecholamine (CA) and protein synthesis inhibitors on memory processing were compared in mice. Diethyldithiocarbamic acid (DDC) and alpha-methyl-p-tyrosine (AMPT) were used as representatives of CA synthesis inhibitors, and cycloheximide (CYCLO) and anisomycin (ANI) as representatives of protein synthesis inhibitors. Four types of brain region were chosen for administration of the drugs: 1) brainstem (site of dopamine) (DA) and norepinephrine (NE) synthesis; 2) caudate and nucleus accumbens septi (major projections of the DA cell bodies in the brainstem; 3) hippocampus, thalamus, or septum (NE projections); and 4) amygdala which contains both DA and NE afferents. Results are consistent with the view that CA neurotransmitters are involved in memory processes, but indicate that CA synthesis inhibitors and protein synthesis inhibitors induce amnesia by different mechanisms. 43 references. (Author abstract modified)

004229 Frey, LeRoy G.; Winter, J. C. Winter: Dept. of Pharmacology and Therapeutics, School of Medicine, State University of New York, Buffalo, NY 14214 **Comparison of the discriminative stimulus properties of nefopam and morphine.** Psychopharmacology. 61(2):231-232, 1979.

The discriminative stimulus properties of nefopam and morphine were investigated in rats. Separate groups of rats were trained to discriminate nefopam or morphine from saline in a two lever operant task. Nefopam produced saline appropriate responding in morphine trained rats. The highest dose of morphine tested in nefopam trained rats produced responding appropriate for neither training treatment. The intermediate morphine responding was antagonized by a naloxone treatment that had no effect on the nefopam discrimination. These results suggest that the stimulus properties of nefopam and morphine are qualitatively different, but also related to those that result in simulus control by nefopam. 7 references. (Author abstract modified)

004230 Frye, Gerald D.; Breese, George R.; Mailman, Richard B.; Vogel, Richard A.; Ondrusek, M. Gene; Mueller, Robert A. Dept. of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **An evaluation of the selectivity of fenmetozole (DH-524) reversal of ethanol-induced changes in central nervous system function.** Psychopharmacology. 69(2):149-155, 1980.

The selectivity and specificity of fenmetozole (DH-524) as an antagonist of the actions of ethanol were examined. Fenmetozole reduced ethanol-induced impairment of the arial righting reflex without changing blood or brain ethanol content, indicating that the antagonistic actions of fenmetozole were not due to change in the pharmacokinetics of ethanol. Since fenmetozole also reduced arial righting reflex impairment due to phenobarbital, chlordizepoxide, and halothane, this action of fenmetozole is not specific to ethanol. In mice, both the ethanol-induced increase in locomotor activity at 2.0g/kg and the decrease caused by 4.0g/kg were antagonized by fenmetozole. In addition, fen-

metozol attenuated the ethanol-induced reduction in cerebellar cyclic guanosine monophosphate (cGMP) content, but the drug also significantly elevated cGMP levels in this tissue when given alone. Fenmetozole did not alter ethanol-induced increases in punished drinking in a conflict test, except at a high dose, which decreased both punished and unpunished responding. Fenmetozole also failed to precipitate ethanol withdrawal like reactions when given to physically dependent, intoxicated rats. Thus, the antagonistic action of fenmetozole against ethanol would not seem to be related to a specific receptor interaction but rather may be the result of a physiological antagonism. 40 references. (Author abstract modified)

004231 Fung, Y. K.; Uretsky, N. J. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **The importance of calcium in amphetamine-induced turning behavior in mice with unilateral nigro-striatal lesions.** Neuropharmacology. 19(6):555-560, 1980.

The role of calcium in the amphetamine-induced turning behavior of mice lesioned with 6-hydroxydopamine was investigated. Instrastriatal administration of either saline or calcium had no effect on amphetamine-induced circling in lesioned mice. In contrast, intrastriatal administration of either EGTA, which chelates extracellular calcium, or verapamil, which inhibits calcium entry into cells, blocked the amphetamine-induced circling. The effect of EGTA was reversed by the administration of calcium to the EGTA solution. At a dose that blocked amphetamine-induced circling, EGTA did not inhibit the circling produced by apomorphine. These results suggest that EGTA may exert its inhibitory effect on amphetamine-induced circling via a presynaptic mechanism. 20 references. (Author abstract)

004232 Garzon, J.; Moratalla, R.; Del Rio, J. Dept. of Pharmacology, Institute of Medicinal Chemistry, CSIC, Juan de la Cierva, 3, Madrid-6, Spain **Potentiation of the analgesia induced in rats by morphine or (D-Ala2)-met-enkephalinamide after inhibition of brain type B monoamine oxidase: the role of phenylethylamine.** Neuropharmacology. 19(8):723-729, 1980.

Morphine and (D-Ala2)-metenkephalinamide induced analgesia in male Wistar rats, reflected an increased reaction time in the tail flick test and an elevated threshold for vocalization induced by tail stimulation. These analgesic effects were potentiated by selective inhibition of brain monoamine oxidase (MAO) type-B with deprenyl or pargyline and were antagonized by selective inhibition of MAO type-A with chlorgyline. Beta-phenylethylamine (PEA), a specific substrate of brain type-B MAO, potentiated the opiate analgesia, especially when combined with deprenyl treatment. The effect of PEA was preferentially related to the affective component of the pain response (vocalization threshold). 30 references. (Author abstract modified)

004233 Gerald, Michael C.; Gupta, Tribhuwan K.; Snider, R. Michael. Division of Pharmacology, College of Pharmacy, Ohio State University, 500 West 12th Avenue, Columbus, OH 43210 **Tolerance to amphetamine-induced impairment of rotarod performance in rats.** Psychopharmacology. 61(3):317-318, 1979.

Tolerance to amphetamine-induced impairment of rotarod performance in rats was investigated. Acute administration of d-amphetamine sulfate caused muscle weakness and 80% failure in rotarod performance in rats. The incidence of performance failure progressively decreased to 30% in animals receiving d-amphetamine and tested daily for 8 days. A similar progressive reduction in performance impairment was observed in animals receiving d-amphetamine for 3, 5, or 7 days (12.5%) and evaluated only once after the last dose. The tolerance is attributable to a physiological or biochemical rather than learning phenomenon. 4 references. (Author abstract modified)

004234 Gisolfi, C. V.; Mora, F.; Wall, P. T. Dept. of Physiology and Biophysics, University of Iowa, Iowa City, IA 52242 **Dopamine and temperature regulation in the primate: effects of apomorphine and pimozide.** Brain Research Bulletin. 5(4):349-352, 1980.

In rhesus and patas monkeys, the dopamine receptor agonist apomorphine (0.05 to 0.6mg/kg) caused a dose related hypothermia associated with salivation, hypermotility, hypersensitivity, pupil dilation, and erection. Pretreatment with the dopamine antagonist pimozide (0.5mg/kg) had no direct effect on body temperatures, but blocked the apomorphine-induced hypothermia. The apomorphine-induced hypothermia appeared to be mediated by an increase in heat dissipation rather than a decline in heat production. 17 references. (Author abstract modified)

004235 Gispen, Willem Hendrik; Ormond, Diana; Ten Haaf, Jeroen; De Wied, David. Div. of Molecular Neurobiology, Institute of Molecular Biology, University of Utrecht, Padualaan 8, Utrecht, The Netherlands **Modulation of ACTH-induced grooming by (Des-Tyr1)-gamma-endorphin and haloperidol.** European Journal of Pharmacology. 63(2/3):203-207, 1980.

Intraventricular administration of the adrenocorticotrophic hormone fragment ACTH1-24 in male Wistar rats induced excessive grooming, which could be blocked by local injection of neuroleptics into the nucleus accumbens or neostriatum. The effect of the neuroleptics was mimicked by (Des-Tyrl)-gamma-endorphin (DTE), but not by alpha-endorphin. The development of acute tolerance to the effect of ACTH1-24 on grooming was reduced by haloperodol or DTE. Results suggest that DTE modulates the dopaminergic activity underlying the display of excessive grooming in animals treated with ACTH. 11 references. (Author abstract modified)

004236 Glick, S. D.; Cox, R. D. Dept. of Pharmacology, Mount Sinai School of Medicine, City University of New York, One Gustave L. Levy Place, New York, NY 10029 **Striatal asymmetry and morphine reinforcement.** Brain Research. 197(1):253-255, 1980.

The hypothesized differential effects of morphine reinforcement on the two sides of the brain were investigated via analysis of the effects of unilateral caudate lesions on morphine self-administration in rats. Results of analysis of both spontaneous and morphine-induced rotations and self-administration data in caudate-lesioned animals indicate that striatal asymmetry is involved in drug reinforcement and that the role of the nigrostriatal system in morphine reinforcement in particular, is not simply a function of activity of the system, but of asymmetry of activity. Reward processes may in general be lateralized and drug-induced euphoria may represent in part a disturbance of lateralization, differential changes in reward sensitivity in the two sides of the brain mediating discriminably different kinds of reward. 11 references.

004237 Glick, Stanley D.; Meibach, Richard C.; Cox, Russell D.; Maayani, Saul. Dept. of Pharmacology, Mount Sinai School of Medicine, City University of New York, One Gustave L. Levy Place, New York, NY 10029 **Phencyclidine-induced rotation and hippocampal modulation of nigrostriatal asymmetry.** Brain Research. 196(1):99-107, 1980.

The effects of phenyclidine (PCP) in eliciting dose related rotation and hippocampal modulation of nigrostriatal asymmetry were investigated. PCP elicited dose related rotation in naive rats. The effect was consistent in direction and magnitude from one week to the next but was dissimilar to the rotatory effects of dopaminergic (D-amphetamine, apomorphine) or anticholinergic (scopolamine) drugs. A study of the effects of PCP on regional brain uptake of labeled 2-deoxy-D-glucose suggests that

PCP-induced rotation is at least in part mediated by an action in the hippocampus. PCP elicited ipsilateral rotation following unilateral hippocampal lesions whereas such lesions did not alter the direction of either nocturnal or D-amphetamine-induced rotation. PCP appears to activate a hippocampal mechanism that normally only modulates the intensity of rotation. 23 references. (Author abstract modified)

004238 Goett, James Michael. Lehigh University **The development of conditioned aversions in pigeons: lithium chloride and delta-9-tetrahydrocannabinol. (Ph.D. dissertation).** Dissertation Abstracts International. 40(3):1399-A, 1979. Ann Arbor, Univ. Microfilms No. 7919974, 91p., 1979.

The question of whether delta-9-tetrahydrocannabinol (THC) can produce conditioned aversions in pigeons, as it does in rats, was investigated. In a series of four experiments, the methodology of producing a conditioned aversion in the pigeon, previously unreported in the literature, was developed. A conditioned aversion was demonstrated using colored water as a conditioned stimulus and lithium chloride as a noxious experience. Experiment 5 used a dose of 2.0mg/kg THC in place of lithium chloride and showed that THC also produces a conditioned aversion in pigeons. The methodological and theoretical implications of a conditioned aversion in the pigeon, and the mechanism of THC's aversiveness are discussed. Issues discussed include: 1) the sensitivity of a two bottle procedure relative to a one bottle procedure; 2) the theoretical importance of a visual cue to aversion theories, and 3) alternative explanations of THC's aversive action. (Journal abstract modified)

004239 Gold, Paul E.; Murphy, James M. Dept. of Psychology, Gilmer Hall, University of Virginia, Charlottesville, VA 22901 **Brain noradrenergic responses to training and to amnestic frontal cortex stimulation.** Pharmacology Biochemistry and Behavior. 13(2):257-263, 1980.

Male Sprague-Dawley rats were trained in a one trial inhibitory avoidance task prior to receiving supraseizure electrical stimulation of frontal cortex, which induces amnesia. Forebrain and brainstem norepinephrine (NE) concentrations decreased by 23% 10 minutes after the footshock training. Posttraining frontal cortex stimulation potentiated the forebrain NE response (31 to 33% below control values) and attenuated the brainstem response (0 to 5% below control values). 58 references. (Author abstract modified)

004240 Gonzalez, J. P.; Sewell, R. D. E.; Spencer, P. S. J. Div. of Pharmacology, Welsh School of Pharmacy, UWIST, Cardiff, Wales **Antinociceptive activity of opiates in the presence of the antidepressant agent nomifensine.** Neuropharmacology. 19(7):613-618, 1980.

Nomifensine showed no antinociceptive activity in the hot plate test in mice, but exerted protective activity comparable to that of morphine in the acid writhing test. The antidepressant caused a marginal degree of antinociception as well as hyperalgesia in the tail immersion test at 48 degrees C, but caused marked hyperalgesia when the temperature was lowered to 45 degrees. This hyperalgesic effect was abolished by the dopamine receptor blocker, haloperidol. Nomifensine augmented the antinociceptive activities of morphine and pentazocine; a 10mcg dose of nomifensine shifted the dose/response curve to the left for morphine, but increased the slope for pentazocine. 29 references. (Author abstract modified)

004241 Gonzalez, Larry P.; Altshuler, Harold L. Dept. of Physiology and Biophysics, University of Illinois Medical Center, P.O. Box 6998, Chicago, IL 60680 **Time-dependent changes in the effects of cholinesterase inhibitors on shuttle-box avoidance.** Pharmacology Biochemistry and Behavior. 12(6):847-850, 1980.

Physostigmine and neostigmine were compared for their effects of shuttle box avoidance acquisition and retention. Physostigmine impaired acquisition at doses lower than neostigmine. Avoidance performance 1, 7, or 14 days after acquisition was impaired by the administration of 0.4mg/kg physostigmine or an equimolar dose of neostigmine. The effects of lower doses of physostigmine, but not of neostigmine, were dependent upon the time of original training relative to drug administration and retesting. Results suggest that the peripheral effects of higher doses of cholinesterase inhibitors impair avoidance performance. The effects of lower doses of physostigmine on acquisition and the time dependent effects on subsequent performance are probably due to the central actions of this drug. 21 references. (Author abstract modified)

004242 Gorelick, David A.; Bridger, Wagner H. Dept. of Psychiatry, University of California, Los Angeles, CA 90024 **Alteration of the facilitatory effect of mescaline by pretreatment with alpha-methyl-p-tyrosine.** Biological Psychiatry. 15(4):619-622, 1980.

The role of catecholamines in mescaline's facilitative effect on a conditioned behavior was examined in rats who were pretreated with alpha-methyl-p-tyrosine (AMPT), an inhibitor of catecholamine synthesis. The experiments indicate that pretreatment with AMPT reduced the mescaline-induced increase in avoidance rate in poor performers by 25% to 50%, although this reduction was statistically significant only at doses 60 and 80mg/kg. These results in conjunction with prior reports that AMPT blocks mescaline-induced increases in locomotor activity suggest that mescaline's facilitative effect on animal behavior is mediated by catecholaminergic systems. AMPT by itself had no disruptive effect in poor performers as measured by either avoidance rate or response latency. All AMPT doses decreased avoidance rate in good performers. 10 references.

004243 Gormezano, I.; Harvey, J. A. Dept. of Psychology, University of Iowa, Iowa City, IA 52242 **Sensory and associative effects of LSD in classical conditioning of rabbit (Oryctolagus cuniculus) nictitating membrane response.** Journal of Comparative and Physiological Psychology. 94(4):641-649, 1980.

Three experiments were conducted to determine the effects of lysergic acid diethylamide (LSD), 30nmol/kg, on the acquisition of the rabbits classically conditioned nictitating membrane response. Experiment 1 revealed that LSD significantly enhanced the acquisition of conditioned responses (CRs), and control groups receiving unpaired conditioned stimulus/unconditioned stimulus (CS/UCS) presentations served to identify LSD's effect to be on learning. In Experiment 1, unconditioned response (UCR) amplitude to a 3 mA USC was not significantly affected by LSD. Moreover, Experiment 2 revealed that LSD had no significant effect on the psychophysical functions relating USC intensity to the frequency or amplitude of the UCRs, and that the drug did not affect the UCS intensity threshold for evoking UCRs. On the other hand, Experiment 3 revealed that LSD significantly enhanced the frequency of CRs to an extended range of CS intensities in the psychological function relating CS intensity to CR frequency. Furthermore, LSD lowered the CS intensity threshold. The drug's enhancement of sensory processing of the CS is postulated to facilitate conditioning through both learning and performance mechanisms. 26 references. (Author abstract modified)

004244 Gray, T.; Wise, R. A. Psychology Dept., Concordia University, 1455 de Maisonneuve Blvd. West, Montreal, Quebec, Canada H3G 1M8 **Effects of pimozide on lever pressing**

behavior maintained on an intermittent reinforcement schedule. Pharmacology Biochemistry and Behavior. 12(6):931-935, 1980.

Lever pressing for food on a variable interval (2.5 min) schedule was challenged by pretreatment with a 1.0mg/kg dose of the dopamine receptor blocker pimozide. Large decreases in response rate were recorded even during the first few minutes of the test session before the rats had received any reinforcement. Pimozide also caused extinction-like effects, but it was clear, from comparisons between pimozide treated rats that were rewarded and pimozide treated rats that were not rewarded, that the rewarding effects of food were not totally blocked. It is suggested that an important aspect of the pimozide produced response decrement is its effect on the incentive motivational properties of food associated apparatus cues known to be important in sustaining responding under extinction and partial reinforcement conditions. 18 references. (Author abstract)

004245 Green, A. R.; Costain, D. W.; Deakin, J. F. W. MRC Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **Enhanced 5-hydroxytryptamine and dopamine-mediated behavioural responses following convulsions -- III. The effects of monoamine antagonists and synthesis inhibitors on the ability of electroconvulsive shock to enhance responses.** Neuropharmacology. 19(9):907-914, 1980.

Behavioral responses mediated by 5-hydroxytryptamine (5-HT) and dopamine (DA) in male Sprague-Dawley rats were enhanced by repeated electroconvulsive shocks (ECS). Studies with various monoamine antagonists and synthesis inhibitors showed that the central noradrenergic system is involved in the ECS-induced enhancement of behavior mediated by 5-HT or DA. The ECS-induced enhancement of DA mediated behavior did not require intact presynaptic DA systems. Intact presynaptic 5-HT systems were necesssary for ECS-induced enhancement of behavior mediated by 5-HT but not that mediated by DA. 42 references. (Author abstract modified)

004246 Halperin, Jeffrey M.; Iorio, Louis C. Dept. of Pharmacology, Schering Corp., 60 Orange St., Bloomfield, NJ 07003 **Protection from shock-induced seizures as a measure of hypnotic potency of drugs.** Pharmacology Biochemistry and Behavior. 13(2):299-301, 1980.

The use of shock-induced seizures to predict the hypnotic potency of drugs was evaluated. Male CF-1 mice were injected with a drug or vehicle and then given a 13mA shock via corneal electrodes. All 15 hypnotics and both antidepressants tested caused dose dependent suppression of seizures; one of the two antihistamines tested also suppressed seizures. Median effective doses for seizure suppression were highly correlated with hypnotic potency in humans. 21 references. (Author abstract modified)

004247 Hammond, E. J.; Hurd, R. W.; Wilder, B. J.; Thompson, Floyd J. Neurology and Medical Research Service, V.A. Medical Center, Gainesville, FL 32602 **Focal and generalized experimental seizures induced by homocysteine.** Electroencephalography and Clinical Neurophysiology. 49(1-2):184-186, 1980.

Electrocorticographic (ECoG) and behavioral effects of parenteral injections of homocysteine in rats are described. Homocysteine activated experimental foci and produced focal seizures in experimental animals with preexisting lesions. It produced generalized ECoG seizures and generalized convulsions in unlesioned animals in higher doses. Of particular interest is the close correlation between electrophysiological discharges and behavior, which is in contrast to other systemic convulsants such as methionine sulphosimine, pentylenetetrazol, and bicuculline. Theoretical and practical advantages of homocysteine-induced seizures as an experimental model of epilepsy are discussed. 7 references. (Author abstract modified)

004248 Harris, R. A.; Snell, Diane; Loh, H. H. Dept. of Pharmacology, University of Missouri, M523 Medical Sciences Building, Columbia, MO 65212 **Effects of chronic d-amphetamine treatment on schedule-controlled behavior.** Psychopharmacology. 63(1):55-61, 1979.

The effect of d-amphetamine added to the drinking water on the rate of conditioned lever-pressing by rats was determined using fixed ratio 30 (FR 30) and fixed interval 2 (FI 2) minute schedules of food presentation. After 32 days of gradual increase in drug concentration the average drug ingestion was 13mg/kg/day. Since acute amphetamine treatment reduced the reinforcement frequency under the FR but not the FI schedule, these results are consistent with the hypothesis that a behavioral tolerance will develop most readily to drug effects that decrease the frequency of reinforcement. 23 references. (Author abstract modified)

004249 Hassmannova, J.; Myslivecek, J.; Romoliniova, A. Myslivecek: IHE, Srobarova 48, 100 42 Prague 10, Czechoslovakia **Learning and memory in the ontogeny of rats given piracetam.** Activitas Nervosa Superior. 22(2):95-96, 1980.

The effect of piracetam, a cyclic GABA analogue, on learning and memory of developing rats was investigated. In 5-week-old animals, no difference occured among control and drug groups in percentage of animals meetings criterion, but there were differences in the number of trials to criterion between drug and control groups. In the 8-week-old group, piracetam increased the percentage of animals meeting criterion and total retrieval from memory. It is noted that 8-week-old rats typically display a decrease in performance in active avoidance learning, and that the facilitory effects of piracetam at this age are more pronounced than at an earlier age. 5 references

004250 Hecht, A. Psychopharmacological Research Laboratory, Dept. E, Sct. Hans Mental Hospital, DK-4000 Roskilde, Denmark **Behavioral effects produced by long-term administration of a neuroleptic drug (flupenthixol) upon social interaction in a group of eight rats.** Psychopharmacology. 62(3):301-305, 1979.

The behavioral effects of chronic treatment with alpha-flupenthixol decanoate followed by a 3 month pause upon social interaction in a group of eight rats were studied. The drug-induced total disruption of two of the group formations studied; the overall behavioral change showed a general depressive effect of the drug and a change in the pattern of social interaction. The shift in balance between the behavioral categories measured appeared as a significant difference in the time spent in the various group formations. An apomorphine test, which concluded the experiment 3 months after the last alpha-flupenthixol decanoate injection, revealed a significant difference in relation to licking response between the test group and the control group. 31 references. (Author abstract modified)

004251 Herling, Seymore; Downs, David A.; Woods, James H. Dept. of Psychology, University of Michigan, Ann Arbor, MI 48109 **Cocaine, d-amphetamine, and pentobarbital effects on responding maintained by food or cocaine in rhesus monkeys.** Psychopharmacology. 64(3):261-269, 1979.

The effects of cocaine, d-amphetamine, and pentobarbital were studied in rhesus monkeys whose lever-press responding was maintained under a second order fixed-interval, fixed-ratio (FI/FR) schedule of food or cocaine reinforcement. Within each session, FI components, ending with the i.v. injection of cocaine (one group of monkeys) or the delivery of a food pellet (second group of monkeys), alternated with FI components

ending without an injection of cocaine or the delivery of food (extinction). Drug pretreatments generally caused comparable dose related decreases in the overall rates of responding reinforced either by cocaine or by food. Response rates during extinction usually increased and then decreased as the dose of each drug increased. Analysis of drug effects on response rates in different temporal segments of the FIs showed that in both the reinforcement and extinction components, the normally low control rates of responding which occurred earlier in the intervals were usually increased, while higher control rates which occurred later in the intervals were increased less or decreased. Thus, the effects of these drugs were relatively independent of the reinforcing event (food or cocaine) and tended to depend more on the ongoing rate of responding under these conditions. 30 references. (Author abstract modified)

004252 Herman, Barbara H.; Leslie, Frances; Goldstein, Avram. Addiction Research Foundation, 701 Welch Road, Palo Alto, CA 94304 **Behavioral effects and in vivo degradation of intraventricularly administered dynorphin-(1-13) and D-A1a2-dynorphin-(1-11) in rats.** Life Sciences. 27(10):883-892, 1980.

Dynorphin-(1-13) induced catalepsy and analgesia in male Wistar rats. The dose required to induce analgesia was at least 10 times higher when the opioid peptide was injected into the lateral ventricle rather than into the cerebral aqueduct. An analogue, D-A1a2-dynorphin-(1-11)., was more stable in brain and more potent than dynorphin-(1-13). The analgesic and cataleptic effects of both compounds were antagonized by pretreatment with naloxone. However, naloxone did not block the bizarre postures, limb rigidity, and barrel rolling induced by lateral ventricular administration of either compound. 23 references. (Author abstract modified)

004253 Hernandez, Linda L.; Powell, D. A. Neuroscience Laboratory, Wm. Jennings Bryan Dorn Veterans' Hospital, Columbia, SC 29201 **Effects of naloxone on Pavlovian conditioning of eyeblink and heart rate responses in rabbits.** Life Sciences. 27(10):863-869, 1980.

Naloxone had no effect on acquisition of the classically conditioned eyeblink response in rabbits, but increased responding during extinction. The drug also attenuated the bradycardiac heartrate conditioned response, suggesting endogenous opioids may be involved in mediating this response. 30 references. (Author abstract modified)

004254 Hicks, P.; Strong, R.; Schoolar, J. C.; Samorajski, T. Texas Research Institute of Mental Sciences, 1300 Moursund Avenue, Texas Medical Center, Houston, TX 77030 **Aging alters amphetamine-induced stereotyped gnawing and neostriatal elimination of amphetamine in mice.** Life Sciences. 27(9):715-722, 1980.

Amphetamine-induced compulsive gnawing was assessed in C57BL/6J male mice (4, 19, and 29 months old). The 29-month-old mice displayed a longer latency before initiation of the compulsive gnawing response and a longer duration of compulsive gnawing response than either younger age group. Following administration of 10mg/kg of 3H-amphetamine sulfate, neostriatal amphetamine levels were equivalent for the first hour for all age groups, but the oldest group of mice had a longer amphetamine elimination half-life from the striatum despite no change in the elimination of amphetamine from the plasma. These changes suggest that in old mice there is an altered time course of stereotyped gnawing response to amphetamine. Also, plasma amphetamine levels may be less reliable as a measure of brain amphetamine levels in old age. 32 references. (Author abstract)

004255 Hoffmeister, Friedrich. Institute of Pharmacology, BAYER AG, Wuppertal-Elberfeld, Germany **Progressive-ratio performance in the rhesus monkey maintained by opiate infusions.** Psychopharmacology. 62(2):181-186, 1979.

Heroin, codeine, dextropropoxyphene, and pentazocine were compared using a drug maintained progressive ratio procedure in the rhesus monkey. Infusions of the drugs were contingent on completion of increasing fixed ratio (FR) response requirements with variable time out periods following each infusion. FR requirements were doubled daily until the number of self-administered infusions per day decreased to less than two infusions. This decrease in the number of infusions is referred to as the breaking point. The dose ranges tested and the resulting breaking point curves are reported. These drug specific dose breaking point functions supplement information on reinforcing properties achieved in other animal experiments and correspond with the clinical pharmacologic information about the abuse liability of the studied drugs. 13 references. (Author abstract modified)

004256 Huidobro-Toro, J. Pablo; Way, E. Leong. Dept. of Pharmacology, New York University Medical Center, 550 First Ave., New York, NY 10016 **Rapid development of tolerance to the hyperthermic effect of beta-endorphin, and cross-tolerance between the enkephalins and beta-endorphin.** European Journal of Pharmacology. 65(2/3):221-231, 1980.

Intracerebroventricular administration of beta-endorphin to male ICR Simonsen mice produced a prompt rise in body temperature that lasted more than 8 hours. The development of tolerance to this hyperthermic effect was rapid and dose dependent for beta-endorphin doses from 10 to 100ng. The development of tolerance was blocked by naloxone. Cross-tolerance to beta-endorphin was seen in animals treated with leucine-enkephalin, methionine enkephalin, or D-Ala2-methionine-enkephalin. 44 references. (Author abstract modified)

004257 Humphries, C. R.; O'Brien, M.; Paxinos, G. Paxinos: School of Psychology, University of New South Wales, P. O. Box 1, Kensington, New South Wales, Australia, 2033 **PCA: effects on ejaculation, thermoregulation, salivation, and irritability in rats.** Pharmacology Biochemistry and Behavior. 12(6):851-854, 1980.

The effects of the short-term monoamine releaser p-chloroamphetamine (PCA) on ejaculation, thermoregulation, salivation, and irritability were investigated in rats. PCA was injected intraperitioneally in male rats housed at 20 degrees C. Within 2 hr of PCA injections, rats showed increased ejaculation, decreased colonic temperature, increased salivation, and increased irritability. Ejaculation and salivation scores were considerably lower in the 2.5mg/kg group than in the higher dose groups (up to 10.0mg/kg), but otherwise were not dose dependent at the doses used. Hypothermia was of similar magnitude in all groups, but lasted longer in the higher dose groups. Irritability increased with dose size. To study the role of ambient temperature in PCA-induced behavioral changes, an additional group of rats housed at the higher ambient temperature of 25 degrees C was observed. In these rats, an increase, rather than a decrease, in mean colonic temperature was observed following PCA injection. Ejaculation and irritability scores were similar to those observed at the lower ambient temperature, but salivation was enhanced. It is suggested that PCA induces ejaculation, salivation, irritability and, depending on the ambient termperature, either hypothermia or hyperthermia. 22 references. (Author abstract modified)

004258 Isseroff, Ami. Section of Neuroanatomy, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510 **Facilitation of delayed spontaneous alternation behavior in adult rats following early hydroxyzine treatment: differential sen-**

sitivity in late infancy. Psychopharmacology. 69(2):179-181, 1980.

When tested in adulthood, male rats that had been treated daily with 50mg/kg hydroxyzine HCl SC at 10 to 29 days or 23 to 29 days of age were significantly facilitated in performance of delayed spontaneous alternation relative to saline injected rats. Treatment at 10 to 16 days of age did not produce significant facilitation in the delay task, nor were there any significant differences between groups in spontaneous alteration with no intertrial delay. The facilitative effect may be attributable to anomalies in areas, such as the limbic system, that continue to develop postnatally and mature in late infancy. It is concluded that delayed spontaneous alternation can be a sensitive behavioral index of changes induced by postnatal drug treatment. 19 references. (Author abstract modified)

004259 Johnson, F. N. Dept. of Psychology, The University , Lancester, England **Effects of lithium on visual perceptual thresholds in the goldfish (Carassius auratus).** Neuroscience Letters. 11:111-114, 1979.

Evidence is presented on the effects of lithium on the visual perceptual thresholds in goldfish (Carassius auratus). Ss show reduced sensitivity to novel visual stimulation following treatment, although the effects were gradually overcome with increasing stimulation. The results are related to a possible effect of lithium on central stimulus analyzing mechanisms. (Journal abstract modified)

004260 Johnsson, G.; Lundborg, P.; Welin-Fogelberg, I. Hassle Research Laboratories, S-43120 Molndal, Sweden **Interaction studies between three antidepressant drugs (chlorimipramine, imipramine and zimelidine) and noradrenaline, tyramine and vagal stimulation on the heart rate and blood pressure in dogs.** Acta Pharmacologica et Toxicologica. 45(3):192-197, 1979.

The effects of noradrenaline, tyramine, and vagal stimulation on blood pressure and heartrate were determined in anesthetized dogs given increasing i.v. doses of imipramine, chlorimipramine, or zimelidine. The in vitro uptake of 5-hydroxytryptamine (5-HT) into platelets after in vivo administration of 5mg chlorimipramine or zimelidine was also examined. Results showed that zimelidine has only slight effects on peripheral adrenergic neurons, compared to imipramine and chlorimipramine. Zimelidine showed less pronounced anticholinergic properties than imipramine but was about equipotent to chlorimipramine in this respect. Zimelidine and chlorimipramine were also equally potent as inhibitors of 5-HT uptake into platelets. Results suggest that zimelidine has high specificty for 5-HT neurons in brain. 22 references. (Author abstract modified)

004261 Jones, R. B. Agricultural Research Council's Poultry Research Centre, King's Buildings, West Mains Rd., Edinburgh EH9 3JS, Scotland **Responses of male and female domestic chicks to a startling stimulus and the effects of a tranquilliser.** Behavioural Processes. 5(2):161-172, 1980.

Sex differences in the responses of domestic chicks to novelty and exposure to a startling reflex were examined. After 10 min in a novel environment, half of a group of 7-day-old chicks were exposed to a loud bell. Males showed more passive behavior such as freezing, sitting, and eye closure, and were less active and less vocal. The second experiment involved injecting males and females with either a tranquilizer (Pacitran) or water. Immobility decreased whereas peeping and walking increased in the Pacitran groups. The behavior of untranquilized, water injected females was comparable to that of Pacitran treated males. These results may reflect sex differences in either the form of fear responding or the underlying levels of fearfulness. 29 references. (Author abstract modified)

004262 Kameyama, Tsutomu; Suzuki, Masahiko; **Nabeshima,** Toshitaka. Dept. of Chemical Pharmacology, **Faculty of Pharmaceutical Sciences,** Meijo University, Tenpaku-ku, Nagoya 468, Japan **Effects of 5-hydroxytryptamine on defecation in open-field behavior in rats.** Pharmacology Biochemistry and Behavior. 12(6):875-882, 1980.

The role of serotonergic fibers in defecation in the open-field by rats as a result of environmental stimulation was investigated via administration of 5-hydroxytryptophan (5-HTP) to stimulate serotonin (5-HT); by intraventricular injection with 5-HT; and by inactivation of the serotonergic neuronal system with p-chlorophenylalanine (pCPA). 5-HTP significantly decreased the number of fecal boluses excreted in both open-field and shuttle box. The fecal excretion was significantly reduced compared with the controls after intraventricular injection of 5-hydroxytryptamine (5-HT). Animals pretreated with pCPA and 5,6-dihydroxytryptamine (5,6-DHT) tended to show a slight increase in open-field defecation. 5-HTP was equally effective in diminishing open-field performance of pCPA treated rats. The inhibitory effects of 5-HTP on the defecation were also observed after depletion of biogenic amines by reserpine treatment. Home cage defecation was increased after 5-HTP administration, decreased under pretreatment with pCPA and not influenced by intraventricular injections of 5-HT. These results suggest that the defecation after environmental stimuli is due to a change in 5-HT levels in the brain. 53 references. (Author abstract modified)

004263 Kari, Ilkka; Rapakko, Seppo; Airaksinen, Mauno M. Dept. of Pharmacy, University of Kuopio, P. O. Box 138, SF-70101 Kuopio 10, Finland **Effect of some beta-carbolines on phenylethylamine and apomorphine stereotypies in rats.** Pharmacology Biochemistry and Behavior. 12(6):979-982, 1980.

The effects of tetrahydro-beta-carbolines (THBCs) and some other beta-carbolines were studied on the stereotypies caused by apomorphine (APO) and phenylethylamine (PEA) in rats. These effects of dopaminergic drugs like apomorphine as well as of PEA have sometimes been used as animal models of paranoid schizophrenia. Dose effect relationships were studied from the most potent substances. All beta-carbolines studied significantly inhibited APO stereotypy. 6-Methoxyharmalan was most effective, followed by beta-carboline (BC), tetrahydro-beta-carboline (THBC), 1-methyl-THBC, y-methoxy-THBC, and 6-hydroxy-THBC. 6-Methoxyharmalan, 6-hydroxy-THBC, and BC also inhibited PEA stereotypy. Results indicate that the mode of PEA and APO stereotypies seems to differ, and beta-carbolines seem to influence these stereotypies by more than one mechanism. If the dopamine hypothesis is valid, the beta-carbolines formed in humans may protect rather than be detrimental in paranoid psychoses. 36 references. (Author abstract modified)

004264 Katz, R. J.; Turner, Barbara B.; Roth, K. A.; **Carroll,** Bernard J. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Central adrenergic neurons as mediators of motivation and behavior-evidence from the specific inhibition of PNMT.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1687-1689).

The role of epinephrine in mediating behavior was examined in male Sprague-Dawley rats. Pharmacological inhibition of the synthetic enzyme phenylethanolamine N-methyltransferase reduced self-stimulation and increased stereotypy and chewing. Epinephrine neurons were also implicated in open field activity and stereotyped running. Results suggest that epinephrine may modulate tonic adrenergic inhibition of dopamine neurons and tonic adrenergic facilitation of self-stimulation. 11 references. (Author abstract modified)

004265 Katz, Richard J. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Behavioral effects of dynorphin -- a novel opioid neuropeptide.** Neuropharmacology. 19(8):801-803, 1980.

Infusion of the neuropeptide dynorphin into the lateral cerebral ventricle of adult male Swiss-Webster mice was followed by an increase in eating and grooming. High doses of dynorphin-induced barrel rotation, sometimes followed by death. The behavioral effects of dynorphin were only partially reversed by naloxone. 4 references. (Author abstract modified)

004266 Katz, Richard J. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Lithium and the structure of exploratory behavior in the rat.** Progress in Neuro-Psychopharmacology. 4(1):37-41, 1980.

The effects of lithium on exploratory behavior of the rat were investigated. Adult male Sprague-Dawley rats were given lithium as a dietary supplement, or a control diet. A single 7 hr test of exploratory behavior was undertaken after 1 week of chronic drug exposure. The structure of exploration was significantly altered by the diet, with experimental animals exploring less intensely and with increased spacing of activity episodes. These findings may represent a useful preclinical analog of some typically observed therapeutic effects of lithium. 18 references. (Author abstract modified)

004267 Katz, Richard J.; Bailey, E. Duff. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **A reexamination of apomorphine-induced stereotypy in the rat in light of self administration experiments.** Progress in Neuro-Psychopharmacology. 3(5/6):483-489, 1979.

The relationship between apomorphine-induced stereotypy and increased self-administration of apomorphine was investigated in rats. Noncontingent intraperitoneal injection of apomorphine in adult male Sprague-Dawley rats immediately prior to their placement in an experimental chamber significantly elevated bar-pressing above operant rates. The role that this novel dopamine enduced behavior plays in self-administration behavior is explored, and three interpretations of this role are evaluated. It is suggested that bar pressing for apomorphine is a function of three variables: reward, stereotypy, and manipulative drive. 14 references. (Author abstract modified)

004268 Katz, Richard J.; Gelbart, Jerry; Carroll, Bernard J. Mental Health Research Institute, Dept. of Psychiatry, University of Michigan Medical Center, Ann Arbor, MI 48109 **Potentiation of L-dopa-induced motor activity by an inhibitor of phenylethanolamine-N-methyltransferase.** Progress in Neuro-Psychopharmacology. 4(1):101-105, 1980.

Pharmacological inhibition of phenylethanolamine-N-methyltransferase (PNMT), the synthesizing enzyme for adrenaline, was found to result in enhanced behavioral activation by 3,4,-dihydroxyphenylalanine (L-dopa) in mice. This suggests that an adrenergic system normally inhibits drug-induced activation and points to an interaction between adrenaline and other catecholamines. Visual observations of these animals indicated that initial injection of SKF 64139 (PNMT inhibitor) induced considerable oral stereotypy, particularly at the highest dose. After L-dopa, the SKF 64139 Ss showed an explosive jumping behavior in which animals would remain by the cage walls and repeatedly jump towards the cage top. 17 references. (Author abstract modified)

004269 Kavaliers, Martin. Dept. of Zoology and Entomology, Colorado State University, Fort Collins, CO 80523 **Circadian rhythm in the effect of theophylline on the behavioral thermoregulation of the white sucker, Catostomus commersoni.** Pharmacology Biochemistry and Behavior. 12(6):843-845, 1980.

The circadian rhythm in the effect of theophylline on the behavioral thermoregulation of the white sucker, catostomus commersoni was investigated. The temperatures selected by white suckers placed in a thermal gradient were significantly altered by interperitoneal injections of theophylline. There was a circadian variation in the effect of theophylline on temperatures selected by individual fish held under constant illumination. Depending on injection time, there was either a significant increase or significant decrease in the temperatures selected. These results are considered in relation to the possible physiological and biochemical effects of theophylline on thermoregulation and circadian rhythms. 21 references. (Author abstract modified)

004270 Kenny, Marie; Leonard, B. E. Biological and Medical Research Institue, P. O. Box 469, James's Street, Dublin 8, Ireland **The effects of strain differences and emotional status of rats on the behavioural and neurochemical effects of chronic treatment with apomorphine.** Progress in Neuro-Psychopharmacology. 4(2):161-170, 1980.

The effects of strain differences and emotional status of rats on the behavioral and neurochemical effects of chronic treatment with apomorphine were investigated. Male Wistar rats, when treated chronically with apomorphine, develop two distinct behavioral responses, namely stereotyped sniffing or ritualized fighting. No correlation was found between emotionality of rats in the open field and the nature of their stereotyped behavior when subsequently treated with apomorphine. Unlike Wistar rats, male Sprague-Dawley rats only exhibited sniffing stereotyped when chronically treated with apomorphine. No correlation was found between the effects of chronic apomorphine administration on brain noradrenaline, serotonin, dopamine, and GABA levels and stereotyped behavior. It appears that Wistar rats are more susceptible to the behavioral and neurochemical effects of apomorphine than those of the Sprague-Dawley strain. 25 references. (Author abstract modified)

004271 Kim, Haing-Ja. Northwestern University **Histochemical fluorescence study of the substantia nigra and role of the nigroneostriatal dopaminergic system in memory and motor functions. (Ph.D. dissertation).** Dissertation Abstracts International. 40(6):2890-B, 1979. Ann Arbor, Univ. Microfilms No. 7927384, 302p., 1979.

Three studies were undertaken to examine the substantial nigra (SN) and the role of the nigroneostriatal dopaminergic system (NDS) in memory and motor function in the rat. Study 1 provided anatomical support for the proposition that dendritic dopamine (DA) in pars reticulate may play a neuromodulatory role, regulating GABA from the neostriatonigral fiber terminals, and supported the notion that the fine fluorescent varicosity containing processes seen in SN pars reticulate are mostly dendritic elements originating from DA cells existing in SN. I study 2, on the effects of passive avoidance retention of 5 min postlearning manipulations of the activity of the NDS using 6-hydroxydopamine (6-OHDA), DA, or gamma-hydroxybutyric acid (GHBA), only 6-OHDA injected into the SN produced a retention deficit; while 5 min postlearning neostriatum injection of DA produced disruption of passive avoidance. These effects were not found when injection was given 22 hr after learning Results suggest that the NDA plays a role in memory consolidation. In study 3, injection of kainic acid produced ipsiversive head tilt and ipsiversive circling followed by contraversive circling and severe contraversive postural assymetry and head rotation the day after injection. Injection of DA or GHBA produced contraversive circling. It is suggested that there may be

at least two neuronal systems in SN which are involved in tonic control of posture. (Journal of abstract modified)

004272 Kitahama, K.; Valatx, J. -L. Departement de Medecine Experimentale, Universite Claude-Bernard, 8, avenue Rockefeller, F-69373 Lyon Cedex 2, France **Instrumental and pharmacological paradoxical sleep deprivation in mice: strain differences.** Neuropharmacology. 19(6):529-535, 1980.

Paradoxical sleep (PS) deprivation was effected by instrumental and pharmacological methods in four inbred mouse strains, C57BR, C57BL/6, BALB/c, and SEC. Instrumental PS deprivation was achieved by the water tank method for 10 to 24 hr. Chlorimipramine, methyl-naphtyl-aziridine, and nialamide were also used to obtain 6 to 24 hr of PS suppression. Later PS rebound was proportional to the duration of PS deprivation but different among strains. In BALB/c and SEC mice, pharmacological deprivation up to 24 hr did not provoke later PS rebound. A single injection of nialamide suppressed PS for about 24 hr, but was not followed by later PS rebound in any of the strains. 30 references. (Author abstract)

004273 Knowles, W. D.; Phillips, M. I. Dept. of Neurological Surgery RI-20, University of Washington, Seattle, WA 98195 **Neurophysiological and behavioral maturation of cerebellar function studied with tremorogenic drugs.** Neuropharmacology. 19(8):745-756, 1980.

In a study of the maturation of the climbing fiber system, the effects of harmaline on the behavior and neurophysiology of developing Sprague-Dawley rats were examined. Neonatal animals showed tremor in response to harmaline at 9.4 days of age. Harmaline induced a bursting pattern of cell firing in the cerebellum at 9.7 days and in the inferior olive at 11.0 days. 44 references. (Author abstract modified)

004274 Koller, W. C.; Weiner, W. J.; Diamond, B. I.; Nausieda, P. A.; Klawans, H. L. Dept. of Neurological Sciences, Rush-Presbyterian St. Luke's Medical Center, 1725 W. Harrison, Chicago, IL 60612 **The pharmacological evaluation of pergolide mesylate as a potential anti-Parkinson agent.** Neuropharmacology. 19(9):831-837, 1980.

Pergolide mesylate, a putative dopamine agonist and potential antiparkinson agent, induced intense behavioral stereotypy in male rats and guinea-pigs, which could be antagonized by haloperidol but not by clozapine. In rats, pergolide reversed the effects of reserpine even after pretreatment with alpha-methyl-p-tyrosine. In dogs, pergolide induced vomiting that could be inhibited by pretreatment with haloperidol. Pergolide produced contralateral rotation in animals with unilateral 6-hydroxydopamine lesions of the substantia nigra. Behavioral subsensitivity to apomorphine developed after 4 weeks of chronic treatment with a low dose of pergolide, but supersensitivity to apomorphine was observed after chronic treatment with higher doses. 19 references. (Author abstract modified)

004275 Kozlowski, Michael R.; Sawyer, Steven; Marshall, John F. Dept. of Psychobiology, University of California, Irvine, CA 92717 **Behavioural effects and supersensitivity following nigral dopamine receptor stimulation.** Nature. 287(5777):52-54, 1980.

The behavioral effects and supersensitivity following nigrostriatal dopamine (DA) receptor stimulation were investigated. Unilateral intranigral injections of the DA receptor stimulant, apomorphine (APO), produced clear contralateral turning in animals that had been previously given intracerebral 6-hydroxydopamine (6-OHDA) injections which extensively damage the ipsilateral nigral DA containing cells, or in animals which had been pretreated for 1 week with the DA receptor blocker, haloperidol. In addition, the turning produced by intranigral APO in 6-OHDA treated animals was much greater when the drug was given 14 to 17 days after the intracerebral neurotoxin than when it was given 4 to 7 days after, suggesting the development of supersensitivity to APO in the nigra. These results suggest that the nigra must be considered as a site of action for drugs whose main effect is on the dopaminergic system. 29 references. (Author abstract modified)

004276 Kromer, Wolfgang; Dum, Jane E. Pharmakologisches Institut der Universitat Munchen, Nussbaumstrasse 26, D-8000 Munich 2, Germany **Mouse-killing in rats induces a naloxone-blockable increase in nociceptive threshold.** European Journal of Pharmacology. 63(2/3):195-198, 1980.

Mouse killing behavior in male Sprague-Dawley rats increased the nociceptive threshold for paw licking in the hotplate test. Naloxone had no effect on the muricidal behavior, but prevented the associated increase in nociceptive threshold. Results suggest that opioid mechanisms may be involved in the changes in nociceptive threshold associated with aggression. 7 references. (Author abstract modified)

004277 Kulkarni, S. K. Dept. of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India **Heat and other physiological stress-induced analgesia: catecholamine mediated and naloxone reversible response.** Life Sciences. 27(3):185-188, 1980.

The role of catecholamines in stress-induced analgesia was studied in Wistar rats and mice via pharmacological manipulations. Acute environmental heat (40 or -2 degrees C) and other physiological stressful situations increased the pain threshold to radiant heat in rats and mice. Naloxone pretreatment or chronic exposure to stress antagonized this response. After pretreatment with catecholamine depeleters, alpha-methyl-p-tyrosine, reserpine or with adrenoceptor blockers, haloperidol, and chlorpromazine, the stress-induced analgesic effect was abolished. Cyproheptadine, a serotonin antagonist, also blocked this response. The results suggest the role of brain monoamines in stress mediated analgesia. 10 references. (Author abstract modified)

004278 Kulkosky, Paul J.; Sickel, Julie L.; Riley, Anthony L. E. W. Bourne Behavioral Research Laboratory, New York Hospital-Cornell Medical Center, 21 Bloomingdale Rd., White Plains, NY 10605 **Total avoidance of saccharin consumption by rats after repeatedly paired injections of ethanol or LiCl.** Pharmacology Biochemistry and Behavior. 13(1):77-80, 1980.

Female Long-Evans rats injected with ethanol or lithium chloride (LiCl) after consuming a novel saccharin solution subsequently drank less saccharin than nonpoisoned controls. A single pairing of saccharin with LiCl or ethanol resulted in partial avoidance of the saccharin solution, and repeated conditioning with LiCl or with high doses of ethanol (3.5 or 5.0g/kg) led to total avoidance of saccharin. Results suggest that the limited consumption of ethanol by rats under ad lib, free choice conditions may reflect an acquired aversion to the oronasal sensory stimuli of ethanol after association with its pharmacologically aversive aftereffects. 40 references. (Author abstract modified)

004279 LaHoste, Gerald J.; Olson, Gayle A.; Kastin, Abba J.; Olson, Richard D. Dept. of Psychology, University of New Orleans, New Orleans, LA 70122 **Behavioral effects of melanocyte stimulating hormone.** Neuroscience and Biobehavioral Reviews. 4(1):9-16, 1980.

The effects of melanocyte stimulating hormone (MSH) on conditioned and unconditioned behavior are reviewed. The isolation, structure, localization, regulation, and biological actions of MSH are also described. Data suggest that MSH influences

the neurological processes involved in attention and related phenomena. 102 references. (Author abstract modified)

004280 Lal, H.; Shearman, G. T.; Fielding, S.; Dunn, R.; Kruse, H.; Theurer, Karin. Dept. of Pharmacology & Toxicology, University of Rhode Island, Kingston, RI 02881 **Evidence that GABA mechanisms mediate the anxiolytic action of benzodiazepines: a study with valproic acid.** Neuropharmacology. 19(8):785-789, 1980.

The anxiolytic effects of valproic acid and diazepam were studied in rats. In male Long-Evans rats trained to discriminate the anxiomimetic agent pentylenetetrazol (1450mcmol/kg) from saline, diazepam (4.4 to 35.0mcmol/kg) and valproic acid (278 to 2220mcmol/kg) both antagonized the anxiomimetic stimulus. In male Wistar rats trained to respond for milk reinforcement and to suppress responses when reinforcement was accompanied by footshock, diazepam (7 to 28mcmol/kg) and valproic acid (1110 to 2220mcmol/kg) antagonized the suppression of responding induced by footshock. These effects were dose dependent and observed at doses that did not result in an overall suppression of responding. Results support the suggestion that GABA mechanisms may mediate the anxiolytic action of benzodiazepines. 29 references. (Author abstract modified)

004281 Lanthorn, Thomas H.; Isaacson, Robert L. University of California, Irvine, CA 92664 **Stretching and yawning: a role of glutamate.** Psychopharmacology. 65(3):317-318, 1979.

In a search for behavior correlates of changes in glutamate mediated neurotransmission, the effect of a glutamate antagonist on the occurrence of stretching and yawning was examined. Systematic injection of glutamate diethyl ester, an antagonist of glutamate and asparate receptors, induced stretching and yawning in rats. This was not accompanied by excessive grooming. Coupled with previous work, these findings suggest that a glutamatergic mechanism is involved in stretching and yawning. 7 references. (Author abstract modified)

004282 Lapin, Izyaslav P. Laboratory of Psychopharmacology, Bekhterev Psychoneurological Research Institute, Leningrad, USSR **Kynurenines and audiogenic excitement in mice.** Pharmacology Biochemistry and Behavior. 13(1):9-15, 1980.

The effects of kynurenines (metabolities of tryptophan on the kynurenine pathway) on audiogenic behavior were studied in three strains of mice. Sound induced locomoter excitement in 73 to 81% of SHR mice, running fits in 33 to 47% clonic convulsions in 15 to 25%, tonic extension in 10 to 22%, and lethality in 7 to 17%. Intraperitoneal injection of 200 to 400mg/kg kynurenine sulfate or 3-hydroxyanthranilic, anthranilic, quinolinic, picolinic, nicotinic or xanthurenic acids decreased this audiogenic excitement, but intraventricular injection of kynurenines (1 to 50mcg) had no effect. Intraventricular injections of kynurenines did not induce an audiogenic response in C57BL/6 or CC57BR mice, which are not normally susceptible to sound. Intraventricular injection of pentylenetetrazol or strychnine did not modify audiogenic excitement, even in near lethal doses. 28 references. (Author abstract modified)

004283 Lapin, Izyaslav P. Laboratry of Psychopharmacology, Behkhterev Psychoneurological Research Institute, Leningrad, USSR **Effect of kynurenine and quinolinic acid on the action of convulsants in mice.** Pharmacology Biochemistry and Behavior. 13(1):17-20, 1980.

Intraventricular injection of DL-kynurenine and L-kynurenine sulfate (40mcg) in conscious SHR mice potentiated the convulsions and lethality induced by strychnine (1mg/kg), but not by thiosemicarbazide or pentylenetetrazol. Quinolic acid, another tryptophan metabolite, had no effect. Intraperitoneal injections of DL-kynurenine induced seizures, and DL-kynurenine prolonged the latency of thiosemicarbazide seizures. Nicotinic, picolinic, and anthanilic acids (100 and 250mg/kg) did not modify the actions of convulsants. The role of brain glycine and GABA receptors in convulsive actions of kynurenines is discussed. 13 references (Author abstract modified)

004284 Latiff, A. A.; Smith, L. A.; Lang, W. J. Dept. of Pharmacology, University of Melbourne, Parkville, Victoria, 3052, Australia **Effects of changing dosage and urinary pH in rats self-administering nicotine on a food delivery schedule.** Pharmacology Biochemistry and Behavior. 13(2):209-213, 1980.

Initial self-administration rates differed in Lister hooded rats given 0.05, 0.1, or 0.25mg/kg nicotine on a food delivery schedule. Once rates of responding were established, no significant changes in responding were observed when doses were changed in all three groups. A decrease in self-administration rate was observed when saline was substituted for nicotine solution after day 18. Initial self-administration rates also differed in rats with alkaline, acidic, or normal urinary pH as a result of drinking sodium bicarbonate solution, ammonium chloride solution, or tap water, respectively. After rates of responding were established at normal urinary pH, however, no significant changes were seen when urinary pH was altered. 12 references. (Author abstract modified)

004285 Le, Anh Dung; Khanna, Jatinder M.; Kalant, Harold; LeBlanc, A. Eugene. Dept. of Pharmacology, University of Toronto, Toronto, Ontario, Canada M5S 1A8. **Effect of L-tryptophan on the acquisition of tolerance to ethanol-induced motor impairment and hypothermia.** Psychopharmacology. 61(2):125-129, 1979.

The effect of L-tryptophan on the acquisition of tolerance to ethanol-induced motor impairment and hypothermia was investigated in rats. Rats were rendered tolerant to ethanol by daily gavage of 4 to 5g/kg ethanol. The degree of motor impairment on the moving belt test and of hypothermia after i.p. test doses of ethanol was measured prior to and at various times during the chronic treatment, to assess the rates of tolerance development. L-tryptophan (75mg/kg twice daily) was administered chronically to elevate brain serotonin level. This treatment did not alter the motor impairment or hypothermia produced by the initial test doses of ethanol. However, the development of tolerance to both the motor impairment and hypothermia effects of ethanol was accelerated in the tryptophan treated rats. This finding complements earlier observations that depletion of serotonin with p-chlorophenylalanine slows down tolerance. Blood ethanol measurements at 20 min (motor impairment) or 90 min (hypothermia) after the administration of the test dose revealed no significaant difference between the control and tryptophan treated rats, suggesting that tryptophan did not influence the metabolism of ethanol. This finding supports the hypothesis that brain serotonin modulates the development of tolerance to ethanol. 25 references. (Author abstract modified)

004286 Leander, J. D. Dept. of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Attenuating the rate-decreasing effects of phenylpiperidine analgesics by pentobarbital.** Psychopharmacology. 63(1):81-88, 1979.

The ability of pentobarbital, diazepam, and chlorpromazine to attenuate the rate decreasing effects of a high dose (10 or 30mg/kg) of meperidine was tested in pigeons responding under a multiple fixed ratio, fixed interval schedule of food presentation. Pentobarbital attenuated the meperidine-induced rate decreases, whereas diazepam or chlorpromazine did not reliably attenuate the response rate decreases. Pentobarbital reliably attenuated the rate decreasing effects of normeperidine, anileridine, and alpha-

prodine, but not the rate decrease induced by fentanyl. The results complement the observations that barbiturates protect animals from the convulsive effects of high doses of meperidine. 32 references. (Author abstract modified)

004287 Leander, J. David. Dept. of Pharmacology, School of Medicine, 231H, University of North Carolina, Chapel Hill, NC 27514 **Effects of propoxyphene, ethoheptazine, and azabicyclane on schedule-controlled responding: attenuation by pentobarbital but not naloxone.** Psychopharmacology. 66(1):19-22, 1979.

The effects of propoxyphene, ethoheptazine, and azabicyclane, both alone and in combination with naloxone, were studied in pigeons responding under a multiple fixed-ratio, fixed-interval (FR/FI) schedule of food presentation. Low doses of pentobarbital attenuated the rate decreasing effects produced by propoxyphene. Low doses of pentobarbital attenuated the rate decreasing effects produced by propoxyphene, ethoheptazine, and azabicyclane. Naloxone antagonized the rate decreasing effects produced by azabicyclane. This suggests that the effects of azabicyclane are due to both narcotic receptors and nonnarcotic systems, and that the effects of propoxyphene and ethoheptazine are due to nonnarcotic sytems. of propoxyphene and ethoheptazine are due to nonnarcotic systems. 19 references. (Author abstract modified)

004288 Leibowitz, S. F.; Rossakis, C. Rockefeller University, 1230 York Avenue, New York, NY 10021 **L-dopa feeding suppression: effect on catecholamine neurons of the perifornical lateral hypothalamus.** Psychopharmacology. 61(3):273-280, 1979.

The effect on catecholamine neurons of the perifornical lateral hypothalamus of L-dopa injections at dosages which produce suppression of feeding in hungry rats (0.8 to 200nM) was investigated. The dose dependent suppression effect was positively correlated in magnitude with the same effect produced by the catecholamine agonists dopamine and epinephrine, and by the catecholamine releasing drug amphetamine. L-dopa's action was partially antagonized by separate injections of the dopaminergic blocker haloperidol (58% blockade) and the beta-adrenergic blocker propranolol (38% blockade). Combined injections of these two antagonists produced a 90% blockade of L-dopa's effect. Periforical administration of the dopa decarboxylase inhibitors Ro4-4602 and MK-486 was also shown to reverse L-dopa's feeding suppression, at doses that enhanced the effect of injected dopamine and epinephrine. On the basis of these findings, L-dopa appears to suppress food consumption in part through increased catecholamine synthesis, specifically within dopaminergic and adrenergic neurons of the perifornical hypothalamic region. 51 references. (Author abstract modified)

004289 Leibowitz, Sarah Fryer. Department of Physiological Psychology, Rockefeller University, New York, NY 10021 **Midbrain-hypothalamic catecholamine projection systems mediating feeding stimulation and inhibition in the rat.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1675-1677).

Studies of the involvement of midbrain/hypothalamic catecholamine (CA) systems in the feeding behavior of rats are summarized. Results suggest there are two anatagonistic CA projection systems to the hypothalamus. One system courses through the dorsal pons and midbrain tegmentum, projects to the paraventricular and periventricular hypothalamic areas, and mediates a stimulatory effect on feeding through alpha-adrenergic receptors. A second system originates in and courses through the ventral midbrain tegmentum, projects to the perifornical hypothalamic area, and mediates a suppressive effect on feeding through dopaminergic and beta-adrenergic receptors. 3 references.

004290 Leppavuori, Antero. Dept. of Physiology, University of Helsinki, Siltavuorenpenger 20, SF-00170 Helsinki 17, Finland **The effects of an alpha-adrenergic agonist or antagonist on sleep during blockade of catecholamine synthesis in the cat.** Brain Research. 193(1):117-128, 1980.

The effects of clonidine (CLO) and phentolamine (PHE) on the sleep/waking cycle of cats treated with alpha-methyl-p-tyrosine (AMPT) alone or combined with atropine were examined. When given alone, 150mg/kg AMPT decreased waking and increased deep slow wave sleep and paradoxical sleep (PS). AMPT did not antagonize the inhibitory effects of CLO or the facilitatory effects of PHE on PS. The increase in PS induced by 20mg/1kg PHE was greater than that seen after AMPT. Atropine reversed the effects of PHE on PS, but did not alter the sleep pattern induced by AMPT. Results suggest that moderate inhibition of catecholaminergic transmission facilitates PS even during a weak blockade of cholinergic receptors. 51 references. (Author abstract modified)

004291 Leppavuori, Antero; Putkonen, Pekka T. S. Dept. of Physiology, University of Helsinki, Siltavuorenpenger 20, SF-00170 Helsinki 17, Finland **Alpha-adrenoceptive influences on the control of the sleep-waking cycle in the cat.** Brain Research. 193(1):95-115, 1980.

Sixteen hour polygraphic sleep recordings were performed in 35 adult cats after i.p. injections of various alpha-adrenoceptor agonists and antagonists. The alpha-agonists clonidine (CLO) and xylazine caused dose dependent increases in paradoxical sleep (PS) and deep slow wave sleep (S2). Alpha-methyldopa suppressed PS, with little effect on other stages. Of the alpha-antagonists, only phentolamine (PHE) significantly increased the 16 hour mean for PS. Thymoxamine (THY) caused a modest, temporary increase in PS. THY and tolazoline (TOL) increased drowsy waking during the first 4 hours and yohimbine (YOH) induced an early increment in aroused waking. Phenoxybenzamine (PBZ) significantly decreased the 16 hour mean for S2 and PS. The suppressant effects of CLO on PS were antagonized by PHE, TOL, and YOH, but the suppressant effects of CLO on S2 were potentiated by THY. PBZ potentiated the suppressant effects of CLO on both PS and S2. 71 references. (Author abstract modified)

004292 Lin, M. T.; Chi, M. L.; Chandra, A.; Tsay, B. L. Dept. of Physiology and Biophysics, National Defense Medical Center, Taipei, Taiwan **Serotonergic mechanisms of beta-endorphin- and clonidine-induced analgesia in rats.** Pharmacology. 20(6):323-328, 1980.

The serotinergic mechanisms of beta-endorphin and clonidine-induced analgesia in rats were investigated. Both beta-endorphin and clonidine significantly increased latency to hind paw lick in the hot plate test. Furthermore, the pain inhibition induced by beta-endorphin and clonidine could be antagonized by prior treatment of animals with either naloxone (a narcotic antagonist) or the depletors of central serotonin pathways such as 5,6-dihydroxytryptamine, 5,7-dihydroxytryptamine, and p-chlorophenylalanine. Naloxone, 5,6-dihydroxytryptamine, 5,7-dihydroxytryptamine, and p-chlorophenylalanine had no effect on latency to hind paw lick. The data indicate that serotinergic activity in the brain plays a role in the elaboration or modulation of beta-endorphin and clonidine analgesia in rats. 32 references. (Author abstract modified)

004293 Lipman, Jonathan J.; Spencer, Paul S. J. Spencer: Div. of Pharmacology, Welsh School of Pharmacy, UWIST, King Edward VII Ave., Cardiff, CF1 3NU, Wales **A comparison of muscarinic cholinergic involvement in the antinociceptive effects**

of morphine and clonidine in the mouse. European Journal of Pharmacology. 64(4):249-258, 1980.

Central or peripheral administration of physostigmine increased the antinociceptive effect (AE) of morphine and clonidine in male mice in a hot water tail immersion test. Atropine sulfate (but not atropine methylnitrate) antagonized the AE of both morphine and clonidine in a dose dependent manner. Oxotremorine produced an AE that was additive but not synergistic with those of morphine and clonidine. Results are discussed in relation to muscarinic cholinergic mechanisms that may be involved in the AE produced by morphine and clonidine. 46 references. (Author abstract modified)

004294 Lovell, D. Karen; Bedford, John A.; Grove, Leatrice; Wilson, Marvin C. Wilson: Dept. of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Effects of d-amphetamine and diazepam on paired and grouped primate food competition.** Pharmacology Biochemistry and Behavior. 13(2):177-181, 1980.

The effects of d-amphetamine (DA, 0.125, 0.5, and 2.0mg/kg) and diazepam (DZP, 0.5 and 2.5mg/kg) on food getting behavior were studied in two male and two female rhesus monkeys. In paired competition studies, submissive animals that normally failed to obtain food were sometimes able to get food when the dominant animal of the pair or both animals were given 0.5mg/kg DA or 2.5mg/kg DZP. Similar effects were observed in group competition, when all four animals were given DA or DZP. 14 references. (Author abstract modified)

004295 Madden, C.; Oei, T. P. S.; Singer, G. Dept. of Psychology, La Trobe University, Bundoora, Victoria 3083, Australia **The effect of schedule removal on the maintenance of heroin self-injection.** Pharmacology Biochemistry and Behavior. 12(6):983-986, 1980.

The effect of schedule removal on the maintenance of heroin self-injection in 80% reduced bodyweight Wistar rats was investigated. During the acquisition phase, 43 animals were subjected to a fixed-time 1 min food delivery schedule and were allowed to self-inject either heroin or saline for 10 days. During the maintenance phase (Days 11 to 15), animals in both the heroin and saline conditions were randomly allocated to schedule, no schedule, and no schedule plus food groups. Infusion rates, hotplate response latencies, and food intake were used as dependent measures to monitor differences between groups. Results reveal that schedule removal disrupts, but does not extinguish, heroin seeking behavior. 13 references. (Author abstract)

004296 Maj, J.; Mogilnicka, E.; Kordecka-Magiera, A. Institute of Pharmacology, Polish Academy of Sciences, 31-343 Cracow, Poland **Effects of chronic administration of antidepressant drugs on aggressive behavior induced by clonidine in mice.** Pharmacology Biochemistry and Behavior. 13(2):153-154, 1980.

Single doses of imipramine, mianserin, or iprindole attenuated the aggression induced by clonidine in male Swiss mice. Chronic administration of these antidepressants enhanced the lonidine-induced aggression. In acute studies, phenoxybenzamine, phentolamine, and propranolol inhibited the drug-induced aggression; metergoline and atrophine had no effect. Results suggest that enhanced noradrenergic transmission may be responsible for the therapeutic activity of antidepressants during long-term treatment. 8 references. Author abstract modified)

004297 Mann, J. F. E.; Boucher, R.; Schiller, P. W. Schiller: Lab of Chem Biology and Peptide Research, Clinical Research Institute, 110 Pine Ave. West, Montreal, Quebec, Canada H2W 1R7 **Rotational syndrome after central injection of C-terminal 7-peptide of cholecystokinin.** Pharmacology Biochemistry and Behavior. 13(1):125-127, 1980.

Intracerebroventricular (i.c.v.) injections of the sulfated C-terminal 7-peptide of cholecystokinin and its N-tert-butyloxycarbonyl protected analog elicited rotational behavior in male Wistar rats. The barrel rotations were accompanied by a lack of additional spontaneous activity, a distorted head and body position, limb flexion and extension, and loss of some reflexes. None of these symptoms was observed after i.c.v. injection of the unsulfated 7-peptide. 23 references. (Author abstract modified)

004298 Marini, J. L.; Walters, J. K.; Sheard, M. H. Connecticut Mental Health Center, P.O. Box 1842, New Haven, CT 06508 **Effects of d- and l-amphetamine on hypothalamically-elicited movement and attack in the cat.** Agressologie. 20(3):155-160, 1979.

The effects of d-amphetamine and l-amphetamine on attack behaviors elicited in the cat by electrical stimulation of the hypothalamus were studied in eight mongrel cats. Stimulation experiments were conducted in a cubic test box, and stimulation was carried out via biphasic square waves. Cats received a 30 min stimulation, followed by injection of saline or saline plus drug, followed by an additional 90 min stimulation. Results show that low doses of d-amphetamine facilitated hypothalamically induced movement and attack; doses of 1.0 to 1.5mg/kg had primarily inhibitory effects. The l-ismoer had facilitory effects at 1.0mg/kg, and was less potent than the d-isomer at 0.25 or 0.50mg/kg. The greater potency of the d-ismoer suggests that a dopaminergic mechanism is important in the behaviors examined. 11 references. (Author abstract modified)

004299 Marrone, B. L.; Rodriguez-Sierra, J. F.; Feder, H. H. Institute of Animal Behavior, Newark, NJ **Intrahypothalamic implants of progesterone inhibit lordosis behavior in ovariectomized, estrogen-treated rats.** Neuroendocrinology. 28:92-102, 1979.

Intracranial implants of crystalline progesterone (P) were used to examine the site of action of P's facilitatory and inhibitory effects on lordosis behavior in the ovariectomized, estradiol-benzoate (EB) primed rat. Progesterone implanted in the medial basal hypothalamus (MBH) 1 hr prior to subcutaneous EB injection inhibited lordosis in response to a systemic progesterone injection 44 h after EB (concurrent inhibition). Progesterone implanted in the MBH did not facilitate lordosis when implanted 44 h after EB injection, but this implant inhibited lordosis in response to progesterone injection 68 h after EB (sequential inhibition). Cholesterol implants in the MBH did not inhibit lordosis in either the concurrent or sequential inhibition paradigms. The results indicate that the MBH is an important site of progesterone inhibition of sexual receptivity in the rat. (Journal abstract modified)

004300 Marsden, C. A. Dept. of Physiology and Pharmacology, Medical School, Queen's Medical Centre, Clifton Blvd., Nottingham NG7 2UH, England **Involvement of 5-hydroxytryptamine and dopamine neurones in the behavioural effects of alpha-methyltryptamine.** Neuropharmacology. 19(8):691-698, 1980.

Alpha-methyltryptamine produced a biphasic behavioral response in male Wistar rats, consisting of hind limb abduction, forepaw treading, lateral head weaving, and Straub tail followed by a period of marked running and exploratory activity. Both behavioral responses were attenuated by p-chlorophenylalanine and alpha-flupenthixol. Metergoline abolished only the initial phase, but fluoxetine prevented the initial response and reduced the second phase. Pimozide had no effect on the first phase, but significantly reduced the exploratory phase. The role of 5-hydroxytryptamine and dopamine neurons in mediating the behav-

ioral response to alpha-methyltryptamine is discussed. 36 references. (Author abstract modified)

004301 Martinez, Joe L., Jr.; Vasquez, Beatriz J.; Rigter, H.; Messing, R. B; Jensen, R. A.; Liang, K. C; McGaugh, J. L. Dept of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **Attenuation of amphetamine-induced enhancement of learning by adrenal demedullation.** Brain Research. 195(2):433-443, 1980.

The effect of immediate posttrial administration of peripherally acting DL-4-hydroxyamphetamine on retention of a one trial inhibitory avoidance response in intact, adrenal medullectomized, sympathectomized, and medullectomized and sympathectomized rats was investigated. In intact rats, 0.82mg/kg of DL-4-hydroxyamphetamine enhanced retention performance. In rats sympathectomized by peripheral 6-hydroxydopamine, 24 h prior to training, a lower dose of 4-hydroxyamphetamine (0.21mg/kg) was most effective in enhancing retention. Adrenal demedulalation abolished the memory enhancing effects of 4-hydroxyamphetamine and also d-amphetamine. These findings suggest that the memory enhancing effects of DL-4-hydroxyamphetamine and d-amphetamine involve adrenal medullary catecholamines. 22 references (Author abstract modified)

004302 Mason, Stephen T.; Beninger, Richard J.; Fibiger, Hans C.; Phillips, Anthony G. Beninger: Dept. of Psychology, University of British Columbia, Vancouver, British Columbia, Canada, V6T 1W5 **Pimozide-induced suppression of responding: evidence against a block of food reward.** Pharmacology Biochemistry and Behavior. 12(6):917-923, 1980.

The pimozide-induced suppression of responding in male albino rats was investigated to evaluate the hypothesis of Wise et al. that pimozide blocks the reinforcing effects of food pellets. Results indicate that the effects of pimozide are additive with those of extinction, so that animals treated with pimozide and placed into extinction cease responding more quickly than animals subjected to either manipulation on its own. In addition, the effects of one condition failed to transfer to the other condition so that animals exposed to three days of pimozide failed to show a further decline when exposed to a day of extinction under vehicle and vice versa. Similar additivity and failure of transfer were seen on a DRL schedule for food reward; however, using this schedule, pimozide failed to produce a decline in reinforced responding. In a further experiment, pimozide failed to mimic extinction by blocking the reinforcing effects of food so as to cause a partial reinforcement extinction effect in a runway. It is concluded that these effects of pimozide on operant behavior are not mediated by a block of reward. 16 references. (Author abstract modified)

004303 Masuda, Y.; Utsui, Y.; Shiraishi, Y.; Karasawa, T.; Yoshida, K.; Shimizu, M. Research Laboratories, Dainippon Pharmaceutical Co., Ltd., Suita-shi, Osaka 564, Japan **Pharmacokinetic and pharmacodynamic tolerance of a new anticonvulsant agent(3-sulfamoylmethyl-1,2-benzisoxazole) compared to phenobarbital, diphenylhydantoin and carbamazepine in rats.** Archives Internationales de Pharmacodynamie et de Therapie. 240(1):79-89, 1979.

Repeated administration of diphenylhydantion (DPH), phenobarbital (PB) and carbamazepine (CB) resulted in the development of tolerance to their anticonvulsant actions against maximal electroshock seizures and to the narcotic action of hexobarbital. No such tolerance was observed following repeated administration of the new anticonvulsant 3-sulfamoylmethyl-1,2-benzisoxazole(AD-810). Pretreatment with an inhibitor of hepatic drug metabolizing enzymes enhanced the anticonvulsant effect and plasma levels of DPH, PB, and CB, but did not alter the anticonvulsant effect or plasma concentration of AD-810. The decreased anticonvulsant activity of DPH and CB following repeated administration appeared to be due to development of pharmacokinetic tolerance, while that of PB was related to both pharmacokinetic and pharmacodynamic tolerance. The lack of tolerance to AD-810 suggests a different mode of metabolism for this drug. 19 references. (Author abstract modified)

004304 Mauron, Charlotte; Wurtman, Judith J.; **Wurtman**, Richard J. Lab. of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Clonidine increases food and protein consumption in rats.** Life Sciences. 27(9):781-791, 1980.

The effects of clonidine on food and protein consumption in rats were investigated. Rats were given clonidine or its diluent, and allowed to eat freely from two isocaloric diets that differed in protein or carbohydrate content. Low clonidine doses (25 to 50mg/kg) significantly increased total food and protein intake by rats given access to a high and a low protein diet. Clonidine's effect was greatest when a diet containing 30% to 45% protein was paired with one that was very low (5%) in protein. In rats given access to only one diet, clonidine administration decreased food consumption when the diet was low in protein, but increased consumption when the diet contained 25% or 50% protein. These data suggest that central noradrenergic synapses participate in the mechanisms controlling appetites for proteins. Clonidine may enhance protein intake by stimulating presynaptic alpha receptors, thus diminishing central noradrenergic tone. Clonidine or related drugs may be useful clinically in treating diseases characterized by impaired appetite or increased need for protein. 18 references. (Author abstract modified)

004305 McDevitt, J. T.; Setler, Paulette E. Dept. of Biological Research, Smith Kline and French Labs., Philadelphia, PA 19101 **Dopaminergic effects of lergotrile: possible involvement of a metabolite.** Neuropharmacology. 19(6):537-542, 1980.

Intraperitoneal administration of lergotrile in rats with unilateral 6-hydroxydopamine lesions of substantia nigra (SNX) was found to produce long lasting contralateral rotation whereas intrastriatal administration of lergotrile failed to cause a rotation response. In intact rats, lergotrile produced intense stereotyped behavior. Both the rotation and stereotypy produced by lergotrile were significantly antagonized by haloperidol or alpha-methyl-p-tyrosine. The production of stereotypy by lergotrile was also antagonized by SK&F 525-A, a microsomal enzyme inhibitory. These studies suggest that a metabolite(s) may be responsible for the dopaminergic effects observed after systemic administration of lergotrile. 22 references. (Author abstract)

004306 McDonald, P. A. Dept. of Zoology, University of British Columbia, Vancouver, British Columbia, Canada **Luteinizing hormone-releasing factor (LRF) and reproductive behavior in male doves exposed to long and short photoperiods.** Neuroendocrinology. 28:151-154, 1979.

To determine if the variable degree of nest building behavior displayed by male doves exposed to different photoregimes is related to differences in luteinizing hormone releasing factor (LRF) levels, androgen treated castrates held on long (16L:8K) or short (8L:16D) daylengths were treated with 20mcg LRF or saline daily. Birds in both groups exhibited higher levels of initial courtship and nest building when held on long days. LRF treatment had no effect on any of the behavior patterns examined. The results suggest that photoperiod does not affect reproductive behavior in male doves through changes in andogenous levels of LRF. (Journal abstract)

004307 McLaughlin, C. L.; Baile, C. A.; Bender, P. E. School of Veterinary Medicine, Pennsylvania University, Philadelphia,

PA **Cannabinols and feeding in sheep.** Psychopharmacology. 64(3):321-323, 1979.

The effects on feeding behavior in sheep of i.v. injections of the d-isomers and l-isomers of delta9-tetrahydrocannabinol (delta9-THC) and 9-aza-cannabinol (9-AC) were investigated. In the first 30 minutes, food intake was increased by the l-isomer of delta9-THC and by 9-AC but was not affected by d-delta9-THC. After 24 hours, feed intake was decreased by at least one dose of d-delta9-THC and l-delta9-THC and 9AC. The l-isomer but not the d-isomer was active at very low doses compared with doses used in many laboratory animals. It is noted that in humans, some component in marihuana other than delta9-THC may override its food intake depressing effect or a receptor system may be affected differently from that in rats or sheep. 16 references. (Author abstract modified)

004308 McLeod, Daniel Roderick. University of Maryland **Effects of d-amphetamine on rates of key-pecking by pigeons exposed to isolated vs. alternating interresponse-time schedules of food presentation. (Ph.D. dissertation).** Dissertation Abstracts International. 40(5):2410-B, 1979. Ann Arbor, Univ. Microfilms No. 7925759, 166p., 1979.

In a series of four experiments, effects of d-amphetamine were assessed on the key-pecking behavior of four pigeons, responding at three separate rates, in the presence of three different response key colors. Highest response rates were unaltered by smaller doses, but were decreased by larger doses of d-amphetamine. Lowest response rates were unaltered or increased by small and intermediate doses, but were only decreased by the largest dose. Effects of d-amphetamine on moderate response rates varied with the context within which the moderate response rates were maintained and with the experimental history of the subjects. Analysis of response rates across all four experiments revealed an inverse relationship between response rate prior to, and response rate following, administration of d-amphetamine. (Journal abstract modified)

004309 Meisch, R. A.; Kliner, D. J. Psychiatry Research Unit, Mayo Box 392, University of Minnesota, Minneapolis, MN 55455 **Etonitazene as a reinforcer for rats: increased etonitazene-reinforced behavior due to food deprivation.** Psychopharmacology. 63(1):97-98, 1979.

Etonitazene reinforced performance was studied in five male Wistar rats who were maintained at 70% of their free feeding weights and who performed lever-presses on a fixed ratio schedule for presentation of water which included up to 5mcg of etonitazene. Performance was increased by food deprivation and decreased by food satiation in spite of the fact that rats normally drink after eating. These changes were not due to general increases in either activity or liquid intake. The results probably reflect generalization of lever-pressing that occurred during the intervening drug session. 5 references. (Author abstract modified)

004310 Mele, Paul C.; Caplan, Marjorie A. Dept. of Psychology, Primate Laboratory, 22 North Charter St., Madison, WI 53706 **Effects of cinanserin and p-chlorophenylalanine and their interaction with d-amphetamine on DRL performance in rats.** Pharmacology Biochemistry and Behavior. 12(6):883-891, 1980.

The effects of the serotonin antagonist cinanserin and the serotonin depletor p-chlorophenylalanine (PCPA) were compared with the effects of d-amphetamine on responding maintained by differential reinforcement of low rate schedule (DRL). d-Amphetamine increased response rates and shortened interresponse times (IRTs). Cinanserin at low doses (8, 16, and 32mg/kg) did not alter DRL responding; high doses (48 and 64mg/kg) decreased response rates and shortened IRTs. PCPA decreased DRL response rates and disrupted the IRT distributions for up to 72 hours postinjection, but had few effects over the subsequent 7 to 8 day period. d-Ampehtamine given in combination with cinanserin or administered 3, 8, and 12 days postPCPA administration resulted in decreased response rates relative to those induced by d-amphetamine alone; the d-amphetamine-induced shortening of IRTs persisted. These results suggest that cinanserin and PCPA do not exert general response stimulant effects and that serotonergic systems are not of major functional significance in the maintenance of low rate DRL responding. These results do suggest that serotonergic systems are involved in the manifestation of the behavioral response to amphetamine, possibly as a result of a serotonergic/catecholaminergic interaction. 59 references. (Author abstract)

004311 Micco, David J., Jr.; McEwen, Bruce S. Rockefeller University, 1230 York Avenue, New York, NY 10021 **Glucocorticoids, the hippocampus, and behavior: interactive relation between task activation and steroid hormone binding specificity.** Journal of Comparative and Physiological Psychology. 94(4):624-633, 1980.

To further delineate whether the observed modulatory effects of adrenal glucocorticoids on appetitive extinction are consistent with adrenal steroid action on hippocampus, adrenalectomized rats were administered corticosterone (C) or dexamethasone (DEX), a synthetic glucocorticoid that is accumulated much less intensively by the hippocampus than is C. While C normalized extinction, DEX did not. In two other hippocampal dependent behaviors, alternation and habituation of exploration as low stress tasks, there was no glucocorticoid modulation of behavior, which may indicate that factors such as the level of activation or the type of learning determine whether a glucocorticoid effect will occur. Findings of a glucocorticoid action on one of three tasks that involve hippocampal function, reinforce the notion that, in addition to their well studied actions in protein and carbohydrate metabolism, the adrenal glucocorticoids may also be subtle modulators of behavior. 29 references. (Author abstract modified)

004312 Moos, F.; Richard, P. Institute of Physiology, University of Strasbourg, Strasbourg, France **Effects of dopaminergic antagonist and agonist on oxytocin release induced by various stimuli.** Neuroendocrinology. 28:138-144, 1979.

Haloperidol, a dopaminergic antagonist, was injected i.p or into the third ventricle (i.c.v.) of lactating rats to determine if a dopaminergic component is involved in the reflex release of oxytocin (OT) induced by vaginal dilation, vagal stimulation, or suckling. The effect of a dopaminergic agonist, apomorphine, on the milk ejection (ME) reflex was also determined. I.c.v. injection of 20mcg haloperidol inhibited the vaginal and vagal reflexes. Inhibition of the ME reflex produced by 2, 5, or 8mg/kg i.p. or by 20 and 40mcg i.c.v. haloperidol was dose dependent. Apomorphine (10mg/kg i.p.) had no effect. The results suggest that a dopaminergic component must be involved in OT release whatever the peripheral stimulus. (Journal abstract modified)

004313 Mora, Sergio; Nasello, Antonia G; Fieschi, Lais. Laboratorio de Medicina Experimental, Faculdade de Ciencias Medicas de Santa Casa de Sao Paulo, Sao Paulo, Brazil **TRH on rat conditioned avoidance behavior: interaction with brain catecholamines.** Pharmacology Biochemistry and Behavior. 13(1):137-139, 1980.

Intracerebroventricular injection of thyrotropin releasing hormone (TRH, 10mcg) improved the acquisition of two way avoidance conditioning in male Wistar rats. This effect was partially antagonized by pretreatment with alpha-methyltyrosine (a-MT, 60mg/kg i.p.) or disulfiram (300mg/kg i.p.). The facilita-

tory effect of TRH was partially was given 2 hours after a-MT. 28 references. (Author abstract restored when L-DOPA (100 mg/kg i.p.) modified)

004314 Morley, John E.; Levine, Allen S. Dept. of Medicine, University of Minnesota, MN 55417 **Stress-induced eating is mediated through endogenous opiates.** Science. 209(4462):1259-1260, 1980.

The interaction of endogenous opiates and stress-induced eating in rats was evaluated by pharmacological manipulation. Eating induced by the tail pinch method was inhibited by the opiate antagonist naloxone. After being repeatedly subjected to stress over a 10 day period and then given naloxone, the rats behaved in a manner indistinguishable from the wet dog shakes of opiate withdrawal. Thus endogenous opiates may have a role in the control of stress related eating, a finding that may have therapeutic implications for humans. 19 references. (Author abstract)

004315 Morris, Michael D.; Burger, Arlen B.; Gebhart, Gerald F. Gebhart: Dept. of Pharmacology, University of Iowa, Iowa City, IA 52242 **Effect of chlordiazepoxide on conditioned and unconditioned fear in rats.** Progress in Neuro-Psychopharmacology. 4(2):153-160, 1980.

The effect of chlordiazepoxide on conditioned and unconditioned fear was investigated in rats. Chlordiazepoxide failed to reduce the conditioned acceleration of a free operant avoidance task to a conditioned stimulus for fear and an unconditioned loud noise stimulus. These results, in conjunction with previous findings, are interpreted to suggest that antianxiety agents do not directly inhibit mechanisms that produce emotional reactions such as fear or anxiety. Instead, these drugs appear to produce their behavioral effects by affecting a serotonergic punishment system and noradrenergic memory system. 35 references. (Author abstract modified)

004316 Mueller, Kathyrne Jean. University of Arizona **Drug-induced self-biting in rodents: implications for the Lesch-Nyhan syndrome. (Ph.D. dissertation).** Dissertation Abstracts International. 41(2):729-B, 1980. Ann Arbor, Univ. Microfilms No. 8017786, 74p., 1980.

The behavioral an biochemical characteristics of drug-induced self-biting in animals are compared with human self-biting in the Lesch-Nyhan syndrome. The behavioral characteristics of three types of drug-induced self-biting (caffeine, clonidine, and pemoline) were examined and then various purines were administered in an attempt o modify self-biting. No evidence was obtained that purines are directly involved in the etiology of drug-induced self-biting. Contrary to expectations, hypoxanthine, a purine found in very high quantities in the central nervous system of Lesch-Nyhan patients, reduced the severity of pemoline-induced self-biting in rats. A hypothesis is advanced that several distinctly different types of self-biting exist, one of which can be described (for both animals and humans) as exaggerated displacement grooming. (Journal abstract modified)

004317 Murphy, James M.; Meeker, Rick B.; Porada, Kenneth J.; Nagy, Z. Michael. Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, IN 46223 **GABA-mediated behavioral inhibition during ontogeny in the mouse.** Psychopharmacology. 64(2):237-242, 1979.

The possibility that GABA systems may mediate some behavioral inhibition during early development was examined in mice 9 to 100 days old injected with the GABA elevating agent amino-oxyacetic acid (AOAA). High levels of locomotor activity characteristic of immature control mice were attenuated following AOAA injection, where as AOAA had little effect on the activity of adult mice. Moreover, AOAA produced a period of rebound hyperactivity for young but not for adult mice. Findings suggest that although GABA systems may mediate early behavioral inhibition, coordination between excitatory and inhibitory capacities matures slowly. In a second experiment, the dopamine-beta-hydroxylase inhibitor FLA-63 prevented rebound hyperactivity in young mice pretreated with AOAA, suggesting that the excitatory component may be mediated by noradrenergic systems. 29 references. (Author abstract modified)

004318 Nielsen, Jann A.; Fossom, Linda H.; Sparber, Sheldon B. Sparber: Dept. of Pharmacology, 3-260 Millard Hall, University of Minnesoata, 435 Delaware St., SE, Minneapolis, NM 55455 **Metabolism of 3H-dopamine continuously perfused through push-pull cannulas in rats' brains: modification by amphetamine or prostaglandin F2alpha.** Pharmacology Biochemistry and Behavior. 13(2):235-242, 1980.

Tritiated dopamine was perfused into the lateral cerebral ventricles of male Long-Evans rats performing an operant task for food reinforcement. Systemic injection of 1.5mg/kg d-amphetamine or 3.0mg/kg l-amphetamine decreased fixed-ratio 20 behavior and reduced levels of tritiated 3-methoxy-4-hydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), and 3-methoxy-4-hydroxyphenylethyleneglycol (MHPG) in the perfusate. Addition of a trace concentration of prostaglandin-F2alpha to the perfusate decreased levels of tritiated DOPAC, HVA, and MHPG, but had no effect on fixed-ratio behavior. 33 references. (Author abstract modified)

004319 Nistico, G.; Di Giorgio, R. M.; Rotiroti, D.; Macaione, S. Institute of Pharmacology, Faculty of Medicine, Piazza XX Settembre, 4 I-98100 Messina, Italy **GABA depletion and GABA-transaminase activity increase after intraventricular 6-hydroxydopamine.** Biochemical Pharmacology. 28(19):3030-3032, 1979.

A single intraventricular injection of 100mcg 6-hydroxydopamine produced a significant decrease in GABA content and a sustained increase in GABA transaminase activity in the diencephalon and brainstem of 1-week-old Rhode Island Red chicks. Behavioral sedation, lethargy, and squatting were also observed. In four of eight chicks, escape responses followed by convulsive episodes were observed within 5 minutes of injection. 26 references.

004320 Nistico, G.; Rotiroti, D.; Naccari, F.; De Sarro, G. B.; Marmo, E. Institute of Pharmacology, Faculty of Medicine, University of Messina, Messina, Italy **Effects of intraventricular beta-endorphin and D-Ala2-methionine-enkephalinamide on behaviour, spectrum power of electrocortical activity and body temperature in chicks.** Research Communications in Chemical Pathology and Pharmacology. 28(2):295-308, 1980.

Behavior, electrocortical activity, and body temperature were studied in Rhode Island Red chicks after injection of beta-endorphin or D-Ala2-methionine-enkephalinamide (DALA) into the third cerebral ventricle. Both peptides caused dose dependent behavioral stupor and hypothermia and decreased reactivity to painful stimuli. Electrocortical high amplitude, slow frequency waves were recorded during behavioral stupor and sedation; total voltage output was increased, with a predominant increase in the lower spectrum frequencies. The hypothermic effects were more marked when chicks were kept in an ambient temperature below their thermoneutral range. Naloxone rapidly reversed the effects of both peptides. 19 references. (Author abstract modified)

004321 Nomura, Yasuyuki; Oki, Keiko. Dept. of Pharmacology, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, Kasumi 1-2-3, Hiroshima 734, Japan **TRH-induced behavioral arousal in developing rats pretreated with 6-**

hydroxydopa. Pharmacology Biochemistry and Behavior. 12(6):925-930, 1980.

The behavioral effect of thyrotropin releasing hormone (TRH) was investigated in the developing rat pretreated with 6-hydroxydopamine (6-OHDA) at birth. An ip injection of TRH increased walking with sniffing, rearing, body shaking, grooming, chewing, and licking in the 7, 14, 20, and 30-day-old as well as in the adult rat. TRH-induced locomotor stimulation began a few minutes after the injection and lasted for approximately 60 min. But on day 7, TRH produced locomotor stimulation between 1.5 hr and 3.5 hr after the injection. Neonatal treatment with 6-OHDA markedly potentiated TRH-induced locomotor stimulation and behavioral arousal in the 7-day-old rat but not in the 14-day-old and adult rat. The marked potentiation of TRH-induced locomotor stimulation by 6-OHDA in the 7-day-old rat was reduced by alpha-flupenthixol and phenoxybenzamine. These results suggest that central dopamine neurons are involved in TRH-induced behavioral arousal in the infant cat. 37 references. (Author abstract modified)

004322 Nutt, D. J.; Green, A. R.; Grahame-Smith, D. G. MRC Unit, Radcliffe Infirmary, Oxford OX2 6HE, England **Enhanced 5-hydroxytryptamine and dopamine-mediated behavioural responses following convulsions -- I. The effects of single and repeated bicuculline-induced seizures.** Neuropharmacology. 19(9):897-900, 1980.

The effects of single and repeated seizures on monoamine function were studied in male Sprague-Dawley rats treated acutely or chronically with bicuculline. Rats treated with bicuculline for 10 days showed enhanced behavioral responses to tranylcypromine (TCP, 5mg/kg) combined with L-DOPA (50mg/kg) or L-tryptophan (75mg/kg) when tested 24 hours after the last bicuculline injection. Responses to TCP/L-DOPA and to apomorphine were also enhanced 24 hours after a single injection of bicuculline, but those to TCP/L-tryptophan were not altered. A single subconvulsive dose of bicuculline failed to enhance the TCP/L-DOPA response. Responses to TCP/L-DOPA were enhanced 24 hours after a single electroconvulsive shock given without anesthesia, but not after shock or bicuculline-induced seizures produced during halotane anesthesia. 17 references. (Author abstract modified)

004323 Ogren, S.-O.; Holm, Ann-Charlotte; Renyi, Anna L.; Ross, S. B. Research and Development Laboratories, Astra Lakemedal AB, S-151 85 Sodertalje, Sweden **Anti-aggressive effect of zimelidine in isolated mice.** Acta Pharmacologica et Toxicologica. 47(1):71-74, 1980.

Zimelidine, a selective serotonin (5-HT) uptake inhibitor, and p-chloramphetamine (PCA), a 5-HT releasing compound, were tested for antiaggressive effects in isolated male NMRI mice. Both agents blocked aggressive behavior in dose that inhibited the accumulation of 14C-5-HT in brain slices, and the time course of behavioral inhibition was related to the drugs' effects on 5-HT mechanisms. Results suggest that zimelidine and PCA inhibit aggressive behavior by enhancing postsynaptic activity in certain 5-HT neuronal pathways. It is suggested that zimelidine may have anxiolytic properties. 18 references. (Author abstract modified)

004324 Panksepp, Jaak; DeEskinazi, Fatma G. Dept. of Psychology, Bowling Green State University, Bowling Green, OH 43403 **Opiates and homing.** Journal of Comparative and Physiological Psychology. 94(4):650-663, 1980.

The effects of pretest administration of opiate agonists and antagonists on acquisition and extinction of social learning homing were examined in four experiments in the young rat. Beginning at 15 days of age, Long-Evans rat pups were trained to run toward their home cage in a T-maze. Morphine (.5 to 1mg/kg subcutaneously) slowed initial acquisition running times, but did not change the number of trials required to learn the position habit. Morphine markedly impeded extinction of the home behavior. Opiate treated animals ran as accurately and as quickly toward home on the 12th day of extinction as on the first (10 trials given per day). Conversely, naloxone (1mg/kg subcutaneously) reduced resistance to extinction. The morphine effect was not state dependent, since the drug also impeded extinction in animals that had acquired the task under saline. The morphine effect was blocked by naloxone, which indicates that the increased resistance was due to an opiate receptor effect. Results indicate that morphine has a strong capacity to sustain a social habit in the absence of reinforcement. 43 references. (Author abstract modified)

004325 Pearson, David E.; Teicher, Martin H.; Shaywitz, Bennett A.; Cohen, Donald J.; Young, J. Gerald; Anderson, George M. Yale University School of Medicine, New Haven, CT **Environmental influences on body weight and behavior in developing rats after neonatal 6-hydroxydopamine.** Science. 209(4457):715-717, 1980.

The effects of varying the litter composition on activity and cognitive performances were examined in normal and 6-hydroxydopamine (6-OHDA) treated rat pups. There was less hyperactive motor activity and better avoidance performance in rat pups treated with 6-OHDA as neonates and reared with vehicle treated littermates than in pups reared in litters composed solely of other 6-OHDA treated animals. It is concluded that an environmental manipulation can provide an alternative to pharmacologic agents in reducing activity and improving learning performance. 18 references. (Author abstract modified)

004326 Pechnick, Robert; Janowsky, David S.; Judd, Lewis. Janowsky: Dept. of Psychiatry, University of California at San Diego, School of Medicine, La Jolla, CA 92093 **Differential effects of methylphenidate and d-amphetamine on stereotyped behavior in the rat.** Psychopharmacology. 65(3):311-315, 1979.

The hypothesis that methylphenidate differs from d-amphetamine not only in its potency, but in its patterns of stereotypy and in its temporal effects was investigated. Different equimolar doses of d-amphetamine and methylphenidate were compared. At lower doses d-amphetamine appeared more effective in causing stereotyped behavior. At higher doses methylphenidate caused more stereotyped behavior at cettain times. It is concluded that an understanding of these differences and a comparison of related biochemical correlates may lead to a better definition of mechanisms underlying psychostimulant effects. 24 references. (Author abstract modified)

004327 Pert, Agu; Moody, Terry W.; Pert, Candace B.; Dewald, Louise A.; Rivier, Jean. Section on Biochemistry and Pharmacology, Biological Psychiatry Branch, NIMH, Bethesda, MD 20205 **Bombesin: receptor distribution in brain and effects on nociception and locomotor activity.** Brain Research. 193(1):209-220, 1980.

Radioreceptor assay of male Sprague-Dawley rat brain showed that the highest concentration of bombesin receptors was associated with limbic forebrain and midbrain structures such as the hippocampus, amygdala, hypothalamus, and periaqueductal gray matter. The caudate/putamen of the extrapyramidal motor system and the forebrain also showed high bombesin binding. Intraventricular injections of bombesin (0.1, 1.0, or 10mcg) produced a dose dependent increase in locomotor activity. Injection of bombesin into the periaqueductal gray produced an antinociceptive reaction in the hot plate and tail flick tests,

but the this analgesia was not antagonized by naloxone. 46 references. (Author abstract modified)

004328 Phillips, Anthony G.; LePiane, Fredrik G. Dept. of Psychology, University of British Columbia, Vancouver, Canada V6T 1W5 **Reinforcing effects of morphine microinjection into the ventral tegmental area.** Pharmacology Biochemistry and Behavior. 12(6):965-968, 1980.

A neural substrate for the reinforcing property of an opiate drug was identified in the ventral tegmental area (VTA) by establishing conditioned reinforcement to salient environmental stimuli paired with intracerebral microinjections of morphine. Bilateral microinjections of morphine in the VTA in doses of 0.2micrograms and 1.0microgram produced a subsequent change in place preference to a distinctive compartment previously associated with the stimulant effects of morphine. Microinjection of 1.0microgram morphine at sites 2.5 mm dorsal to the VTA had no effect. Pretreatment with naloxone antagonized the reinforcing effects of morphine as this group showed no significant change in place preference. Nor did control groups receiving microinjections of sterile physiological saline. Taken together, these data suggest that opiate receptors, located in the ventral tegmental area, play an important role in mediating the reinforcing effects of morphine. The possible involvement of dopaminergic neurons in these effects is discussed. 19 references. (Author abstract)

004329 Phillips, Anthony G.; LePiane, Frederick G. Dept. of Psychology, University of British Columbia, Vancouver, British Columbia, Canada V6T 1W5 **Disruption of conditoned taste aversion in the rat by stimulation of amygdala: a conditioning effect, not amnesia.** Journal of Comparative and Physiological Psychology. 94(4):664-674, 1980.

Two experiments were conducted to determine whether the disruption of conditioned taste aversion (CTA) by delivery of amygdaloid brain stimulation (BS) during conditioning could be attributed to the stimulus properties of the BS. In Experiment 1, animals receiving BS while drinking saccharin, during the onset of lithium chloride (LiCl) toxicosis, or in the interval between taste exposure and toxicosis drank significantly more saccharin solution during a 48 hr retest than implanted or unoperated controls receiving similar taste/toxicosis pairings. In contrast, a group receiving BS during both conditioning and retention trials developed a strong CAT. Experiment 2 confirmed that amygdaloid stimulation can form a compound with the taste of the saccharin solution. A small but significant aversion was displayed by groups exposed to BS plus taste during conditioning and to either taste alone or BS alone during the retest. Again, the group presented with BS and taste prior to and following LiCl toxicosis displayed a strong conditioned aversion. These data suggest that the disruption of CTA with basolateral nucleus amygdaloid stimulation represents a conditioning effect, not amnesia. 31 references. (Author abstract)

004330 Pilc, A.; Nowak, J. Z. Institute of Pharmacology, Polish Academy of Sciences, 31-343 Krakow, 12 Smetna Str., Poland **The influence of 4-methylhistamine, an agonist of histamine H2 receptors on body temperature in rats.** Neuropharmacology. 19(8):773-775, 1980.

The histamine H2-receptor agonist 4-methylhistamine produced a dose dependent hypothermia when injected into the lateral ventricles of female Wistar rats. This effect was antagonized by cimetidine, an H2-receptor antagonist. The effect of 4-methylhistamine was abolished at an ambient temperature of 32 degrees C. The thermoregulatory behavior of rats injected with 4-methylhistamine tended to compensate for the fall of body temperature. It is concluded that the hypothermic action of 4-methylhistamine is due to stimulation of heat loss pathways. 17 references. (Author abstract modified)

004331 Plech, A. Dept. of Pharmacology, Biological-Physiological Institute, Silesian Medical Academy, Katowice, Poland **The influence of microinjections of cholinomimetics into hypothalamus on the locomotor activity of rats.** Agressologie. 20(D):279-282, 1979.

The role of the central cholinergic system of the hypothalamus in the regulation of rats' locomotor activity was studied. Acetylcholine (ACh), carbachol, nicotine, eserine, and atropine were injected bilaterally into different areas of rat hypothalamus, and immediate behavioral effects were observed. ACh injected into the anterior hypothalamus significantly inhibited locomotor activity, but previous intraperitoneal injections of atropine prevented such inhibition from occurring. Injections of ACh into the medial or posterior portions of the hypothalamus had no significant effect on locomotor activity, nor did bilateral injections of carbachol or nicotine. The results suggest that cholinergic neurons in anterior hypothalamus are important in the regulation of locomotor activity of rats, but further studies to determine their character are necessary. 7 references. (Author abstract modified)

004332 Pradhan, S. N.; Bhattacharyya, A. K.; Pradhan, Sikta; Aulakh, C. S. Dept. of Pharmacology, Howard University College of Medicine, Washington, DC **Dopaminergic-serotoninergic roles in behavioral effects of psychomotor stimulants and cannabis.** Psychopharmacology Bulletin. 16(2):52-54, 1980.

The effects of psychomotor stimulants (e.g., amphetamine and cocaine) and delta 9-tetrahydrocannabinol on three behavioral schedules (self-stimulation, spontaneous motor activity, and stereotypy) of rats were examined to investigate the roles of central neurotransmitters in the behavioral effects of drugs of abuse. Levels of four central neurotransmitters (norepinephrine; dopamine; DA, serotonin; 5-HT, and acetylcholine) were also assessed in discrete brain areas (caudate nucleus; diencephalon/midbrain; and pons/medulla). It appears that the stimulant and depressant phases of the effects of these drugs might be correlated with increase and decrease in the DA levels and reverse changes in 5-HT levels, respectively, in the relevant brain areas. 8 references.

004333 Przegalinski, Edmund; Baran, Leokadia; Palider, Wladyslaw; Siwanowicz, Joanna. Dept. of Pharmacology, Institute of Pharmacology, Polish Academy of Sciences, 12 Smetna Street, 31-343 Krakow, Poland **The central action of pizotifen.** Psychopharmacology. 62(3):295-300, 1979.

The central action of the potential antidepressant drug pizotifen was examined in mice, rats, and rabbits. Pizotifen in doses up to 10mg/kg was ineffective in classic tests for antidepressant activity. It neither antagonized the effects of reserpine in rats nor potentiated the effects of amphetamine, nialamide or L-dopa on locomotor activity. Pizotifen inhibited the head twitch reaction induced by L-5-hydroxytryptophan in mice and by 5-methoxytryptamine in rats. Pizotifen inhibited or abolished LSD or quipazine-induced stimulation of the hindlimb flexor reflex of spinal rats; the effect was not due to noradrenolytic action of the drug. It is suggested that pizotifen strongly blocks the central postsynaptic serotonin receptors. 38 references. (Author abstract modified)

004334 Puglisi-Allegra, Stefano; Mack, Gerard; Oliverio, Alberto; Mandel, Paul. Lab. di Psicobiologia e Psicofarmacologia, Via Reno, 1, I-00198 Rome, Italy **Effects of apomorphine and sodium Di-n-propylacetate on the aggressive behaviour of three strains of mice.** Progress in Neuro-Psychopharmacology. 3(5/6):491-502, 1979.

The effects of apomorphine and sodium Di-n-propylacetate (DPA, sodium valproate) on pain-induced aggressive behavior were investigated in three inbred strains of mice which exhibited spontaneously low levels of aggression: BALB/c, C57B1/6, and DBA/2. Apomorphine elicited aggressive behavior in the three strain; the range of effective doses was different for each strain. DPA was effective in inhibiting apomorphine elicited aggression but the three strains exhibited a different sensitivity to this drug. The effects of DPA were not related to pain sensitivity, posture and locomotion. Only C57 strain exhibited a slight postural and locomotor impairment when injected with a higher dose of DPA. Results are discussed in terms of a genetic inference and of biological differences existing between these three strains. 47 references. (Author abstract modified)

004335 Rackham, Anita. Pharmacology Dept., Merck Frosst Laboratories, Kirkland, Quebec, Canada **Opiate-induced muscle rigidity in the rat: effects of centrally acting agents.** Neuropharmacology. 19(9):855-859, 1980.

Muscle rigidity induced by morphine and etonitazine in female Sprague-Dawley rats was reduced by cyclobenzapine, chlorpromazine, and zoxazolamine. Benzodiazepines (diazepam, fletazepam, and oxazepam) were ineffective against the supraspinally mediated opiate effects, as were haloperidol, perphenazine, L-DOPA, apomorphine, pentobarbital, and atropine. It is suggested that reduction of opiate-induced muscle rigidity in rats may be used as an index of muscle relaxant properties of agents with supraspinal sites of action. 10 references. (Author abstract modified)

004336 Radulovacki, Miodrag; Wojcik, Walter J.; Fornal, Casimir; Miletich, Robert. Dept. of Pharmacology, College of Medicine, University of Illinois, Chicago, IL 60680 **Elimination of REM sleep rebound in rats by alpha-adrenoreceptor blockers, phentolamine and phenoxybenzamine.** Pharmacology Biochemistry and Behavior. 13(1):51-55, 1980.

Two alpha-adrenoreceptor blocking agents, phentolamine (5mg/kg i.p.) and phenoxybenzamine, (10mg/kg i.p.) abolished the REM sleep rebound normally observed in male Sprague-Dawley rats deprived of REM sleep for 24 hours. The white brain concentration of 3-methoxy-4-hydroxyphenylethyleneglycol sulfate was increased in these animals, suggesting the drugs produced an effective central alpha-adrenergic receptor blockade. Results suggest that a reduction in noradrenergic transmission may abolish REM sleep rebound. 27 references. (Author abstract modified)

004337 Ramirez, J. Martin; Delius, Juan D. Psychologisches Institut, Ruhr-Universitat, Bochum, Germany **Behavioral effects of intracerebroventricular infusion of luteinizing hormone releasing hormone (LH-RH) in pigeons.** Bulletin of the Psychonomic Society. 16(2):128-130, 1980.

Pigeons were implanted with stainless steel cannulae in the lateral ventricles of the brain and infused with different concentrations of luteinizing hormone releasing hormone (LHRH) and CF insulin (a decapeptide with a quite different structure), as well as with saline, in counterbalanced order. LHRH elicited dose dependent effects in animals' behavior and CF insulin resulted in much weaker reactions; the saline infusion generally had no behavioral effects. Results failed to provide any substantive evidence for consistent changes in aggression or more generally agonistic behavior, except that this group of behaviors, as well as feeding, drinking, preening, and courting behaviors, were suppressed by a behavioral syndrome involving eye blinking, neck twisting, head shaking, and wing shivering (weakest response) to jerking shivers, rigidity, and complete loss of balance (strongest response). Comparative doses of both decapeptides elicited different degrees of responses; CF insulin at best yielded only a weak effect. 28 references. (Author abstract modified)

004338 Raskin, Lisa A. Princeton University **A behavioral analysis of the ontogeny of amphetamine anorexia. (Ph.D, dissertation).** Dissertation Abstracts International. 40(3):1416-A, 1979. Ann Arbor, Univ. Microfilms No. 7919779, 82p., 1979.

The behavioral components of feeding which underlie the transition in the effect of amphetamine on food intake during ontogency were assessed in the rat. At 5 days of age, amphetamine had no effect on either contact time with the mother, nursing time, or activity levels. By 15 days of age, nursing behavior was significantly disrupted but contact time and activity levels remained unaffected. At 25 days of age, treated pups spent less time in contact with and nursing from the mother and exhibited significantly higher levels of activity than littermate controls. Amphetamine facilitated approach to the mother at all ages but disrupted nipple attachment when pups were 15 days or older. When fed via a tongue cannula, pups of all ages exhibited an anorectic response to amphetamine. It was also confirmed that this anorectic response seen in the 5-day-old was not simply a function of stereotyped motor response competing with the pup's ability to ingest the infused diet. The results suggest the functional maturity of neurochemical systems mediating amphetamine anorexia in the young pup. (Journal abstract modified)

004339 Rauca, Ch.; Kammerer, E.; Matthies, H. Dept. of Pharmacology and Toxicology, Medical Academy, DDR-301 Magdeburg, Germany **Choline uptake and permanent memory storage.** Pharmacology Biochemistry and Behavior. 13(1):21-25, 1980.

The uptake of tritiated choline and its incorporation into tritiated acetylcholine (ACh) was studied in hippocampal slices from male Wistar rats with good or poor long-term memory. Labeled choline uptake and incorporation into 3H-ACh was higher in hippocampus slices from rats that showed good retention of a brightness discrimination than in those with poor retention. Results indicate individual differences in cholinergic activity in the hippocampus can influence retention in individual animals. 36 references. (Author abstract modified)

004340 Rawlins, J. N. P.; Feldon, J.; Gray, Jeffrey A. Gray: Dept. of Experimental Psychology, University of Oxford, South Parks Road, Oxford OX1 3UD, England **Discrimination of response-contingent and response-independent shock by rats: effects of chlordiazepoxide HCL and sodium amylobarbitone.** Quarterly Journal of Experimental Psychology. 32(Part 2):215-232, 1980.

Rats, trained to press a lever for sucrose reward on a random interval (RI) schedule, were presented while lever pressing with two stimuli, each associated with a different schedule of shock delivery: in the presence of one stimulus (Sc), shock occurred irrespective of the rat's behavior; in the presence of the other (Sp), shocks were programmed on the same schedule, but delivered only when the rat pressed the lever. Both stimuli suppressed lever pressing. In addition, the rats developed significantly different response rates in the two stimuli, thus demonstrating a discrimination between response contingent and response independent shock. Group data showed faster responding in Sc than in Sp, supporting the view that response contingent shock produces greater suppression than response independent shock. Individual animal analyses, however, demonstrated that this was the case in the majority of animals, but not in all. Response suppression was alleviated by amylobarbitone sodium (15 mg/kg) or chlordiazepoxide HC1 (5 mg/kg); the latter drug alleviated suppression significantly more in Sp than

Sc and eliminated the difference between the response rates controlled by the two stimuli. 20 references. (Author abstract)

004341 Reitzel, J.; Oppenheim, R. W. Oppenheim: Neuroembryology Laboratory, North Carolina Division of Mental Health, Dorothea Dix Hospital, Raleigh, NC 27611 **Ontogeny of behavioral sensitivity to glycine in the chick embryo.** Developmental Psychobiology. 13(5):455-461, 1980.

Strychnine (STR), glycine (GLY), and GABA were injected intravenously into 6 and 7 day chick embryos and subsequent effects upon spontaneous motility were observed. In 7-day-old embryos, STR alone increased motility and when injected simultaneously with GLY, antagonized the GLY-induced motility decrements; STR did not antagonize GABA-induced motility decrements. In 6 day embryos, STR injected alone had no effect on motility, but did antagonize motility decrements induced by simultaneous injection of GLY but not those induced by GABA. Results are consistent with the contention that GLY mediated inhibitory mechanisms become functional in the chick spinal cord on about the seventh day of incubation. The possibility that the presynaptic terminal may precede, and possibly play a role in the development of the postsynaptic GLY (or STR) receptors is considered. 21 references. (Author abstract modified)

004342 Reyes-Vazquez, Cruz; Brust-Carmona, Hector. Depto. de Fisiologia, Div. de Investigacion, Facultad de Medicina, UNAM, Aplo. Postal 70250, Mexico 20, DF Mexico **Facilitation of the suppressing effect of dopamine upon a motor conditioned response by 6-hydroxydopamine applied to the caudate nucleus in cats.** Pharmacology Biochemistry and behavior. 13(1):97-101, 1980.

The role of catecholamines in the caudate nucleus (CN) in the inhibitory actions required for the suppression of motor responses was confirmed in cats. Animals were trained to press a lever to obtain milk when a conditioned discriminative stimulus (light) was on and to supress the reponse when the light was off. Bilateral application of dopamine (DA) to the CN produced a decrement in lever-pressing only in the suppression situation. Pretreatment with 6-hydroxydopamine enhanced the effects of DA. 24 references. (Author abstract modified)

004343 Riffee, William H.; Wilcox, Richard E.; Smith, Robert V. Dept. of Pharmacology and Drug Dynamics Institute, College of Pharmacy, University of Texas, Austin TX 78712 **Modification of drug-induced behavioral arousal by preinjection routines in mice.** Psychopharmacology. 63(1):1-5, 1979.

The effects on drug-induced behavioral arousal in mice of environment (home cage versus a novel environment), injection routine, and handling was studied. Prior injection of a saline solution 1 hour before injection of dextroamphetamine and apomorphine (experimental group) or saline solution (control group) resulted in substantially less behavioral arousal in the control groups following the second saline injection. With saline preinjection, the differences in behavioral arousal were maximized, statistical variance minimized, and an orderly time/response relationship observed. A novel environment, even with saline preinjection, introduced a variable that caused differences in behavioral arousal induced by a low dose of dextroamphetamine, but not by apomorphine. It is concluded that these factors can conceal behavioral arousal (locomotor activity, repetitive movements, and rearing) as detected by an electromagnetic sensor. 8 references. (Author abstract modified)

004344 Risch, Craig; Kripke, Daniel; Janowsky, David. Department of Psychiatry, University of California at San Diego, Medical School, La Jolla, CA 92093 **Flurazepam effects on methylphenidate-induced stereotyped behavior. (Unpublished paper).** Research Report, NIMH Grant 1P50-MH-30914, 1979. 16 p.

The effects of flurazepam (0.0, 0.5, and 3.0mg/kg) on methylphenidate-induced increases in stereotypy, gnawing, sniffing, and locomotion were evaluated in Swiss-Webster mice in daytime and nighttime experiments. Methylphenidate (50mg/kg) caused an increase in overall stereotypy and in stereotyped gnawing behavior; and methylphenidate (25mg/kg and 50mg/kg) caused a significant increase in locomotion and sniffing behavior. Flurazepam (3.0mg/kg) significantly augmented methylphenidate-induced stereotyped gnawing behavior and stereotypy. Flurazepam significantly decreased locomotion and sniffing, but did not interact with methylphenidate's effects on locomotion and sniffing. 15 references. (Author abstract)

004345 Rodgers, R. J. Postgraduate School of Studies in Psychology, University of Bradford, Bradford BD7 1DP, England **Effects of nicotine, mecamylamine, and hexamethonium on shock-induced fighting, pain reactivity, and locomotor behaviour in rats.** Psychopharmacology. 66(1):93-98, 1979.

Three series of experiments were performed to evaluate possible nicotinic cholinergic influences on fighting behavior in rats. Each series consisted of three tests (naive animals in each test): shock-induced fighting, pain threshold estimation, and locomotor activity. In the first series, nicotine was found to produce a dose dependent inhibition of fighting without altering shock thresholds. However, the highest dose used also significantly reduced rearing in the activity test. In the second series, mecamylamine (a centrally active antinicotinic) produced a facilitation of fighting at low doses and an inhibition at higher doses. While these effects are unrelated to changes in shock threshold, the high dose resulted in a reduction in both horizontal activity and rearing. Finally, as a control for possible peripheral effects of nicotinic blockade, a third series examined the behavioral effects of hexamethonium. Low doses of this compound had little effect on fighting, while higher doses attenuated these responses. Although hexamethonium had no effect on shock thresholds, the highest dose produced a facilitation of horizontal activity. Results are discussed in relation to the hypothesis of central nicotinic cholinergic inhibition of agonistic behavior. 38 references. (Author abstract modified)

004346 Rolinski, Z.; Kozak, W. Dept. of Pharmacology, Institute of Physiological Sciences, Agricultural Academy, 20-033 Lublin, Poland **The role of the catecholaminergic system in foot-shock-induced fighting in mice.** Psychopharmacology. 65(3):285-290, 1979.

The role of the catecholaminergic system in foot-shock-induced fighting aggression in mice was studied with the help of behavioral tests and biochemical experiments. The administration of the catecholamine precursor L-dopa combined with enzymatic decomposition inhibitors as well as dopamine agonists produced increases in the number of fighting episodes in mice. Catecholamine synthesis inhibitors, clonidine, and noradrenaline synthesis inhibitors depressed the number of fighting episodes. Higher noradrenaline utilization in the brain was found in aggressive mice. Results suggest a significant role of noradrenaline dopamine in producing the foot-shock-induced fighting aggression in mice. 47 references. (Author abstract modified)

004347 Romer, Dietmar; Buscher, Heinz; Hill, Ronald C.; Maurer, Richard; Petcher, Trevor J.; Welle, Henk B. A.; Bakel, Herman C. C. K.; Akkerman, Antony M. Preclinical Research Dept., Sandoz Ltd., Basal, Switzerland **Bremazocine: a potent, long-acting opiate kappa-agonist.** Life Sciences. 27(11):971-978, 1980.

Tests in mice, rats, and rhesus monkeys showed that bremazocine, a benzomorphan analogue, is a potent, centrally acting analgesic with a long duration of action. It showed no physical or psychological dependence liability and did not induce respiratory depression. The compound's pharmacological profile suggests it is an opiate kappa-receptor agonist. 22 references. (Author abstract modified)

004348 Rosic, N.; Bokonjic, D.; Overstreet, D. H. Overstreet: School of Biological Sciences, Flinders University of South Australia, Bedford Park, South Australia 5042 **Task-dependent development of tolerance to scopolamine.** Pharmacology Biochemistry and Behavior. 13(2):183-186, 1980.

Task dependent tolerance to scopolamine was demonstrated in male Wistar rats given 0.5mg/kg/day scopolamine for 21 days. When tested 48 hours after cessation of chronic treatment, these animals did not differ from saline controls in spontaneous locomotor activity or acquisition of active avoidance of a two-way shuttlebox. The increase in locomotor activity induced by acute treatment with scopolamine was smaller in rats chronically treated with scopolamine was smaller in rats chronically treated with scopolamine than in the saline group. However, the acute scopolamine treatment facilitated the acquisition of active avoidance responding to an equivalent degree in rats treated chronically with scopolamine or saline. 16 references. (Author abstract modified)

004349 Ruffing, Diane; Kovacic, Beverly; Demetriou, Sandra; Domino, Edward F. Dept. of Pharmacology, Lafayette Clinic, 951 E. Lafayette, Detroit, MI 48207 **Naloxone enhancement of DMT and LSD-25 induced suppression of food-rewarded bar pressing behavior in the rat.** Psychopharmacology. 62(3):207-210, 1979.

The effects of the interaction of naloxone with N,N-dimethyltryptamine (DMT) and lysergic acid diethylamide-25 (LSD) on the bar-pressing behavior of male Holtzman rats were examined. LSD or increasing doses of DMT were administered i.p. to disrupt food rewarded bar-pressing. Pretreatment with behaviorally ineffective doses of naloxone dramatically enhanced the effects of DMT and LSD. There was no significant difference for either brain or liver 14C-DMT levels when control DMT rats were compared with the naloxone pretreated rats. It is concluded that the results seem to rule out interference by naloxone with the metabolism of DMT as a mechanism of the observed behavioral potentiation. 30 references. (Author abstract modified)

004350 Rusterholz, David B.; Dryer, Stuart E.; Long, John Paul; Barfknecht, Charles F.; Mott, James. Dept. of Chemistry, Indiana University, 1125 East 38th St., Indianapolis, IN 46205 **Sedative and analgesic actions of methoxylated 2-aminotetralins involvement of alpha1- and alpha2-adrenoreceptors.** European Journal of Pharmacology. 65(2/3):201-211, 1980.

In tests for sedation and analgesia in male Swiss-Webster mice, three 5,8-dimethoxylated derivatives of 2-aminotetralin (2-AT) were less potent than clonidine, but more potent than methoxamine or phenylephrine. Yohimbine antagonized the effects of clonidine and a 2-AT derivative in both tests, suggesting the involvement of alpha2-adrenoceptors in these behavioral effects. The inhibition of exploratory activity induced by methoxamine was antagonized by phenoxybenzamine but not yohimbine; this suggests that alpha-adrenoceptors may also be involved in sedation. 48 references. (Author abstract modified)

004351 Ruthrich, Heide-Linde; Wetzel, Wolfram; Matthies, Hansjurgen. Institute of Pharmacology and Toxicology, Medical Academy, DDR-301 Magdeburg, Germany **Postnatal orotate treatment: effects on learning and memory in adult rats.** Psychopharmacology. 63(1):25-28, 1979.

During the postnatal period, male Wistar rats were treated with orotate, either from the 6th to 15th, 16th to 25th, or 26th to 35th days of life. Learning and memory were tested in adulthood. Rats that received orotate early showed better retention of a learned brightness discrimination than controls. An active avoidance was leearned more quickly as well. The results suggest that memory retention in adulthood can be improved by postnatal orotate treatment. 19 references. (Author abstract modified)

004352 Sahakian, B. J.; Growdon, J. H.; Millington, W. R.; Barr, J. K.; Wurtman, R. J. Department of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **An animal model of pharmacological therapy for tardive dyskinesia using cholinergic drugs.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1614-1616).

To test an animal model of tardive dyskinesia (TD), the intensity of apomorphine-induced stereotyped behavior (A-ISB) was determined in male Sprague-Dawley rats given apomorphine and a direct or indirect cholinergic agonist. Cholinergic agonists that directly stimulate central muscarinic receptors, such as pilocarpine, suppressed A-ISB even when given in doses too low to produce a detectable effect on acetylcholine (ACh) levels. Single doses of indirectly acting cholinergic agonists, such as physostigmine and choline chloride, did not antagonize A-ISB unless given in doses large enough to produce immobility. However, these drugs increased striatal ACh levels and their chronic administration might eventually block A-ISB. It is concluded that A-ISB is a useful animal model for determining the efficacy of agents in the alleviation of symptoms of TD, but that a chronic administration paradigm might provide a more powerful model than the acute administration used in this study. 13 references. (Author abstract modified)

004353 Sanger, D. J.; Greenshaw, A.J.; Thompson, I. P.; Mercer, J. D. Dept. of Pharmacology, Reckitt and Colman, Pharmaceutical Division, Dansom Lane, Hull, HU8 7DS, England **Learned taste aversion to saccharin produced by orally consumed d-amphetamine.** Pharmacology Biochemistry and Behavior. 13(1):31-36, 1980.

Female Wistar rats developed taste aversions to solutions of saccharin (1mg/ml) containing amphetamine at concentrations of 0.01, 0.03, or 0.1mg/ml. A taste aversion conditioned to a solution of 2mg/ml saccharin and 0.2mg/ml ampetamine generalized to solutions containing saccharin concentrations of 0.625 to 20mg/ml, but not to a solution containing only amphetamine. When the saccharin concentration in conditioning trials was 0.625mg/ml, the aversion generalized to concentrations as low as 0.75mg/ml, but aversion did not generalize to concentrations below 2mg/ml when a 10mg/ml solution was used for conditioning. 20 references. (Author abstract modified)

004354 Sansone, Mario. Laboratorio di Psicobiologia e Psicofarmacologia, C.N.R. Via Reno 1, I-00198 Rome, Italy **Effects of repeated administration of chlordiazepoxide on spontaneous locomotor activity in mice.** Psychopharmacology. 66(1):109-110, 1979.

The effects of repeated administration of chlordiazepoxide on spontaneous locomotor activity were investigated. Mice were treated with single or repeated doses (five daily injections) of chlordiazepoxide, and subjected to a 60 minute activity test on day 5, 15 minutes after the last daily injection. The repeated administration enhanced the stimulatory action of the lower doses of the drug, while the depressant effect of the higher doses was

reduced. It is concluded that tolerance develops to the depressant but not to the excitatory effects of chlordiazepoxide, so that the stimulatory action of the drug on locomotor activity appears stronger after repeated administrations. 14 references. (Author abstract modified)

004355 Satake, Nobuhiro. Bekesy Laboratory of Neurobiology, University of Hawaii, Honolulu, HI 96822 **Effect of S-adenosylhomocystein on color avoidance behavior.** Pharmacology Biochemistry and Behavior. 13(2):305-306, 1980.

Intracranial injection of the hydroxyindole-O-methyltransferase inhibitor S-adenosylhomocystein (SAH) prior to color avoidance training in goldfish caused a delay in responding to a white or green conditioned stimulus in the shuttlebox. The latency of responses to red or blue stimuli was not altered. Results suggest that SAH increased preference for white and green, but did not increase general brightness preference. 7 references. (Author abstract modified)

004356 Schallert, Timothy; Overstreet, David H.; Yamamura, Henry I. Dept. of Psychology, University of Texas, Austin, TX 78712 **Muscarinic receptor binding and behavioral effects of atropine following chronic catecholamine depletion or acetylcholinesterase inhibition in rats.** Pharmacology Biochemistry and Behavior. 13(2):187-192, 1980.

Muscarinic receptor binding and locomotor responses to atropine were studied in male Sprague-Dawley rats given intraventricular infusions of the catecholamine neurotoxin 6-hydroxydopamine (6-OHDA) or chronically treated with diisopropylfluorophosphate (DFP), an irreversible acetylcholinesterase inhibitor. Atropine slightly decreased locomotion in control rats but caused excessive forward walking in animals made akinetic by 6-OHDA. The binding of 3H-quinuclidinyl benzilate (QNB) to membrane preparations was not altered in the 6-OHDA treated animals. Atropine failed to induce excessive forward motion in the DFP treated rats, which did show decreased 3H-QNB binding. The DFP treated rats developed tolerance to the locomotor suppressive effects of DFP, cross-tolerance to the cholinergic agonist pilocarpine, and exaggerated atropine-induced increases in core temperature and stereotypy. 40 references. (Author abstract modified)

004357 Schechter, Martin D. Dept. of Pharmacology, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272 **Caffeine potentiation of apomorphine discrimination.** Pharmacology Biochemistry and Behavior. 13(2):307-309, 1980.

In rats trained to discriminate between apomorphine (0.1mg/kg i.p.) and saline in a two lever, food motivated operant task, apomorphine produced dose related drug appropriate responding, but caffeine (7.5 to 3.0mg.kg) produced saline appropriate responding. However, caffeine (15mg/kg) potentiated the discriminative stimulus properties of low doses (0.01, 0.02, and 0.04mg/kg) of apomorphine. This potentiation was antagonized by pretreatment with 0.25mg/kg haloperidol. It is suggested that caffeine, which is a phosphodisterase inhibitor, increases postsynaptic cyclic AMP and leads to supersensitization of dopamine receptors. 11 references. (Author abstract modified)

004358 Schiff, Stanley R.; Bridger, Wagner H.; Sharpless, Nansie S.; King, James J. Dept. of Psychiatry, Albert Einstein College of Medicine, Bronx, NY **Conditioning using drugs affecting dopaminergic systems as unconditioned stimuli: behavioral and biochemical evidence.** Psychopharmacology Bulletin. 16(2):24-27, 1980.

The possibility that drugs affecting dopaminergic systems might serve as unconditioned stimuli, and the hypothesis that dopaminergic activity is responsible for this conditioning was investigated. Male Long-Evans hooded rats were given 10 daily sessions of tone paired with intraperitoneal drug injection. Various doses of d-amphetamine sulfate (AMP) apomorphine hydrochloride (APO), or haloperidol (HAL) were used. The ten daily conditioning sessions were followed on the 11th day by one session for the assessment of conditioning during which placebo replaced drug. APO failed to demonstrate significant conditioned behavior following the pairings, but clear conditioning of AMP-induced stereotypy and hyperactivity was observed. Clinical implications are noted. 9 references.

004359 Schiff, Stanley Raymond. Yeshiva University **Classical conditioning of d-amphetamine- and apomorphine-induced behavior in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 41(2):529-B, 1980. Ann Arbor, Univ. Microfilms No. 8018026, 136p., 1980.

To examine the possibility that d-amphetamine (AMP) and/or apomorphine (APO) induced stereotypy and hyperactivity could be classically conditioned, male Long-Evans hooded rats were given 10 daily training trials of tone paired with intraperitoneal drug injection, one of three doses of AMP or APO. The chronic effects of AMP, as determined by behavioral analysis of the conditioned groups over the 10 daily training trials, consisted of significant tolerance to AMP-induced increased activity and potentiation of AMP-induced stereotypy over trials. APO-induced hyperactivity and stereotypy showed no significant changes over the 10 daily training trials. These chronic drug results confirm the findings of previous studies. For the AMP groups, increases of head bobbing, sniffing, horizontal locomotor activity and rearing were clearly conditioned. For the APO groups, head bobbing and sniffing showed conditioned increases. APO is shown to be a weaker stimulus for conditioning since the pooling of all the APO dosage groups was necessary to demonstrate significant conditioning of fewer behaviors. (Journal abstract modified)

004360 Schiorring, Erik. Psychopharmacological Research Laboratory, Sct. Hans Mental Hospital, Dept. E, DK-4000 Roskilde, Denmark **Social isolation and other behavioral changes in groups of adult vervet monkeys (Cercopithecus aethiops) produced by low, nonchronic doses of d-amphetamine.** Psychopharmacology. 64(3):297-302, 1979.

The effects of low, nonchronic doses of d-amphetamine on social isolation and other behaviors of groups of adult vervet monkeys (Cercopithecus aethiops) were investigated. Doses of d-amphetamine (0.1 to 0.7mg/kg body weight) were administered to three independent groups, each group consisting of a triad of one male and two females. Amphetamine changed both the individual and the social behavior patterns significantly. Stereotypy and social isolation (withdrawal) were characteristic features of the amphetaminized animals. Also stereotyped social grooming was observed. Results are discussed in relation to behavior changes seen in amphetamine psychoses. It is emphasized that the study of patterns of behavior is an important object of research and a relevant line in future investigation of human psychopathology. 55 references. (Author abstract modified)

004361 Schmidt, W. J.; Meierl, G. Biologisches Institut der Universitat, Ulmer Strasse 227, D-7000 Stuttgart 60, Germany **Antidepressants and the control of predatory behavior.** Physiology & Behavior. 25(1):17-19, 1980.

The predatory behavior of adult male ferrets was not inhibited by chronic treatment with imipramine or acute treatment with fluoxetine or chlorimipramine. The drugs did induce piloerection and increase the amount of biting. Results are contrasted to previous studies demonstrating a marked inhibition of

muricidal behavior in rats treated with antidepressants. 24 references. (Author abstract modified)

004362 Schmidt, Werner J. Biologisches Institut, Abteilung Tierphysiologie, Ulmerstrasse 227, D-7000 Stuttgart 60, Germany **Effects of d-amphetamine, maprotiline, L-dopa, and haloperidol on the components of the predatory behavior of the ferret, Putorius furo l.** Psychopharmacology. 64(3):355-359, 1979.

The effects of d-amphetamine, maprotiline, L-dopa, and haloperidol on components of the predatory behavior of the ferret, Putorius furo l., were examined. One hour before ferret predation on rats was examined in an arena, one of the drugs was administered. Provided that capture was successful, the sequence of the behavior was not changed by these drugs. With the exception of paw movements and rolling over, which were not affected by the drugs, the components of predatory behavior were influenced differently. This supports the assumption that a drug affects different mechanisms which control behavior. It is concluded that dopamine is involved in the control of capture elicitation as well as in the control of pursuit and biting. Capture elicitation was inhibited by d-amphetamine and L-dopa, but not by maprotiline, and was facilitated by haloperidol. The orientation of pursuit movements and biting was impaired by L-dopa and improved by haloperidol, whereas maprotiline did not influence these components. 28 references. (Author abstract modified)

004363 Scraggs, P. R.; Baker, H. F.; Ridley, R. M. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, Middlesex, HA1 3UJ, England **Interaction of apomorphine and haloperidol: effects on locomotion and other behaviour in the marmoset.** Psychopharmacology. 66(1):41-43, 1979.

The behavioral effects of increasing doses of apomorphine and haloperidol were observed in a group of six marmosets. Behavior was classified quantitatively into categories: locomotion, inactivity, checking (small head movements), social interaction, and purposeful activities. Statistical analysis reveals that apomorphine has a stimulant effect on checking and locomotion which can be antagonized by haloperidol. Activities and social contact were severely reduced by both apomorphine and haloperidol. Inactivity was increased by the lowest dose of apomorphine in otherwise untreated animals. It is suggested that haloperidol antagonizes the stimulant effects of apomorphine but is synergistic to its suppressant effects, and that the low dose effect of apomorphine on inactivity is mediated by a mechanism which may be different from that acted upon by haloperidol. 13 references. (Author abstract)

004364 Segal, D. S.; Kelly, P. H.; Koob, G.; Roberts, D. C. S. University of California, San Diego, La Jolla, CA 92093 **Nonstriatal dopamine mechanisms in the response to repeated d-amphetamine administration.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1672-1674).

The effects of 6-hydroxydopamine lesions of the nucleus accumbens septi on spontaneous and d-amphetamine-induced activity were examined in rats. Spontaneous activity was reduced for 7 days after the lesion. The locomotor response to d-amphetamine (0.5, 1.0, 2.5, and 5.5mg/kg) was significantly decreased 11 days after the lesion, but the stereotypic response was not altered. Repeated administration of d-amphetamine (0.5mg/kg) augmented the behavioral response to the drug in sham injected controls but not in lesioned rats. Results suggest that the mesolimbic dopamine system is not required for the expression of amphetamine-induced stereotypy, but is required for the occurrence of d-amphetamine-induced locomotion and for augmentation of the behavioral response to d-amphetamine. 11 references. (Author abstract modified)

004365 Seiden, L.; Erinoff, L.; MacPhail, R.; Heller, A.; Miller, F. E. Department of Pharmacological and Physiological Sciences, University of Chicago, Chicago, IL 60637 **Age-dependent effects of 6-hydroxydopamine on locomotor activity in rats.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1669-1671).

The effect of brain dopamine depletion on locomotor activity was examined in rats. Animals were pretreated with desmethylimipramine prior to administration of 6-hydroxydopamine (6-HDA) at 3 and 6 days, 11 and 14 days, 20 and 23 days, or 46 and 48 days postpartum. Rats treated at 46 and 48 days postpartum showed no change in locomotor activity, but animals treated at younger ages showed persistent hyperactivity. The animals treated with 6-HDA at 3 and 6 days also had a supersensitive response to L-DOPA when tested at 20 to 35 days of age; low doses of L-DOPA caused a large increase in locomotor activity, while high doses had no effect. The role of striatal and cortical dopamine in the expression of locomotor activity is discussed. 4 references. (Author abstract modified)

004366 Seppala, T.; Palva, E.; Mattila, M. J.; Korttila, K.; Shrotriya, R. C. Dept. of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Tofisopam, a novel 3,4,-benzodiazepine: multiple-dose effects on psychomotor skills and memory. Comparison with diazepam and interactions with ethanol.** Psychopharmacology. 69(2):209-218, 1980.

Twelve healthy male volunteers were treated (double-blind crossover design) with tofisopam (a new 3,4-benzodiazepaine), diazepam, or placebo, on two consecutive days each. Psychomotor skills were impaired after a single dose of diazepam given on day 1. Measurements on day 2 showed that some tolerance had developed to the diazepam-induced impairment of reactive and coordinative skills, but not to its effects on flicker fusion or on the extracular muscle balance. Tofisopam failed to impair performance both as a single dose and after repeated doses. Ss reported more fatigue, dizziness,calmnes, and passiveness after diazepam than breath ethanol concentrations were 0.6 to 1.0mg/ml and all psychomotor skills were impaired. Diazepam plus ethanol particularly impaired memory and learning as well. After this combination, Ss were classified (time anticipation test) as disqualified drivers more often than after placebo. It is concluded that diazepam, as well as either benzodiazepine with ethanol, may reduce the ability to drive vehicles or operate machinery. 23 references. (Author abstract modified)

004367 Shannon, Harlan E.; Holtzman, Stephen G. Holtzman: Dept. of Pharmacology, Emory University School of Medicine, Atlanta, GA 30322 **Morphine training dose: a determinant of stimulus generalization to narcotic antagonists in the rat.** Psychopharmacology. 61(3):239-244, 1979.

The effect of morphine training dose on stimulus generalization to narcotic antagonists in the rat was investigated. Rats were trained to discriminate between saline and either 1.75mg/kg or 5.6mg/kg of morphine in a two choice discrete trial avoidance paradigm. Both groups of rats generalized completely to higher doses of morphine as well as to profadol and pentazocine, analgesics with narcotic antagonist properties. The dose of each test drug required to elicit drug appropriate responding was about one half log unit higher in the rats trained with 5.6mg/kg morphine than in the rats trained with 1.75mg/kg. Rats trained with the lower dose of morphine also generalized completely to the narcotic antagonist nalbuphine and to the nonopioid drug d-amphetamine, and generalized partially to the narcotic antagonist cyclazocine. In contrast, rats trained with

the higher dose of morphine showed only partial generalization to nalbuphine and virtually none to cyclazocine and d-amphetamine. The degree of stimulus generalization to the narcotic antagonists and to d-amphetamine in the two groups of rats corresponds well with the known similarities and differences between the syndromes of subjective effects engendered by these drugs and morphine in man. These results indicate that systematic variation of the morphine training dose can facilitate characterization of the discriminative stimulus properties of narcotic antagonist analgesics and enhance the value of drug discrimination procedures as a model for predicting the subjective effects of these drugs. 24 references. (Author abstract modified)

004368 Sheard, Michael H. Connecticut Mental Health Center, 34 Park Street, New Haven, CT 06508 **The role of drugs affecting catecholamines on shock-elicited fighting in rats.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1690-1692).

The effects of amphetamine, phentolamine, apomorphine, clonidine, propranolol, phenoxybenzamine, and piperoxane on shock elicited fighting were examined in male Sprague-Dawley rats. Clonidine and propranolol both significantly inhibited fighting. A low dose of piperoxane increased fighting, but a larger dose inhibited fighting. No significant effects were observed with the other drugs. Results suggest that reactive aggression can be understood as a balance of central action on adrenergic (locus coeruleus) and serotonergic (raphe) neurons. 9 references. (Author abstract modified)

004369 Shearman, Gary; Lal, Harbans. Lal: Dept. of Pharmacology and Toxicology, University of Rhode Island, Kingston, RI 02881 **Descriminative stimulus properties of pentylenetetrazol and bemegride: some generalization and antagonism test.** Psychopharmacology. 64(1):315-319, 1979.

The discriminative stimulus properties of pentylenetetrazol (PTZ) and bemegride were investigated in male hooded rats. Animals were trained to respond on a FR 10 schedule of food reinforcement via levers associated with drug or saline injections. All of 14 Ss learned to descriminate reliably between the effects of 20mg/kg PTZ and saline. Seven of eight rats learned to discriminate between the effects of bemegride (5mg/kg) and saline. None of the rats learned to discriminate between 5mg/kg PTZ and saline. The bemegride discriminative stimulus generalized to PTZ (20mg/kg) and was antagonized by chlordiazepoxide. Chlordiazepoxide, diazepam, flurazepam, clobazam, and ceprobamate were all effective antagonists of PTZ in a dose dependent manner. Bemegride end cocaine generalized to the PTZ discriminative stimulus in a dose dependent manner, but d-amphetamine, methylphenidate, and nicotine did not. Since bemegride and PTZ are convulants at higher doses, the discriminative stimulus properities of these drugs might be based on a subtle convulsive brain state. The anxiolytic properites of benzodiazepines and meprobamate suggest that the discriminative stimulus produced by these convulsants is related to an anxiety inducing action. 36 references. (Author abstract modified)

004370 Simansky, Kenny Jay. University of Iowa **The roles of serotonin and norepinephrine in the modulation of pain sensitivity in the rat. (Ph.D. dissertation).** Dissertation Abstracts International. 40(5):2423-B, 1979. Ann Arbor, Univ. Microfilms No. 7924529, 303p., 1979.

The relative involvement of serotonin (5-HT), norepinephrine (NE), and dopamine (DA) in the nociceptive reactions of rats to foot shock and direct heating of the foot pads was examined. The effects of impaired monoaminergic function were assessed with chronic selective or combined depletions of 5-HT, NE, and DA produced by electrolytic lesions of the medical forebrain bundle or intrahypothalamic or intraventricular injections of neurotoxins either alone or after treatment with desipramine. The effects of enhanced monoaminergic function were also evaluated. Taken together, the results establish that NE and 5-HT normally suppress responses to different types of noxious stimuli. Thus, 5-HT suppresses the jump response to shock, and NE the paw lick response to heat. These data therefore emphasize that an organism's response to pain is determined by the integration of a number of separable processes. It is proposed that 5-HT mediates reflexes subserving phenomena known as fast or first pain in humans, while NE subserves second or slow pain. (Journal abstract modified)

004371 Sloviter, Robert S.; Connor, John D.; Damiano, Bruce P.; Drust, Eugene G. Dept. of Pharmacology, Milton S. Hershey Medical Center, Pennsylvania State University, Hershey, PA 17033 **Para-halogenated phenethylamines: similar serotonergic effects in rats by different mechanisms.** Pharmacology Biochemistry and Behavior. 13(2):283-286, 1980.

The p-chloro, p-chloro-beta-methyl, p-fluoro, p-bromo, and p-iodophenethylamine derivatives produced a behavioral syndrome (serotonin syndrome) in male Sprague-Dawley rats similar to that induced by p-chloroamphetamine (PCA). However, these halogenated phenethylamines did not deplete brain serotonin as did PCA. Pretreatment with p-chlorophenylalanine (PCPA) prevented the serotonergic effects of both chloro derivatives and partially prevented the effects of bromophenethylamine and iodophenthylamine; 5-Hydroxytryptophan restored behavioral responses to these compounds in PCPA treated rats. PCPA did not prevent the behavioral effects of p-fluorophenethylamine. Zimelidine prevented the serotonergic behavioral effects of all compounds tested except p-fluorophenethylamine. 18 references. (Author abstract modified)

004372 Smith, James B. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Prevention by naltrexone of tolerance to the rate-decreasing effects of morphine on schedule-controlled responding in the pigeon.** Psychopharmacology. 63(1):49-54, 1979.

Keypecking in the pigeon was maintained under 10 minute fixed-interval and 30 response fixed-ratio schedules of food presentation in a study to determine whether the antagonist naltrexone would block the development of tolerance to the rate decreasing effects of morphine on the responding of pigeons. Naltrexone alone had no systematic effect of responding and morphine practically eliminated responding. When naltrexone regularly preceded daily injections of morphine, tolerance was prevented for some dose combinations but not for others. There were doses of naltrexone which completely antagonized the acute effects of morphine but which did not prevent tolerance development. Differences in prevention of tolerance by doses of naltrexone that antagonized the acute effects of morphine were probably due to differences in duration of effect. 9 references. (Author abstract modified)

004373 Smith, James B. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **Behavioral influences on tolerance to the effects of morphine on schedule-controlled behavior.** Psychopharmacology. 66(1):105-107, 1979.

Behavioral influences on tolerance to the effects of morphine on schedule controlled behavior were investigated. Responding of pigeons was maintained under a multiple fixed-interval, fixed-ratio schedule of food delivery, and 10mg/kg morphine was administered daily. Responding during both schedule components was initially decreased and measurable tolerance developed to this effect after four daily injections. However, the rate of tolerance development differed depending on whether or not pres-

ence of the drug coincided with performance during experimental sessions. Tolerance developed more rapidly when morphine was given before daily experimental sessions than when morphine was given daily, but animals did not perform daily in experimental sessions. Tolerance to the rate decreasing effects of morphine depended on relations between presence of the drug and exposure to experimental sessions. 8 references. (Author abstract modified)

004374 Smith, L. A.; Lang, W. J. Dept. of Pharmacology, University of Melbourne, Parkville, Victoria, 3052, Australia **Changes occurring in self administration of nicotine by rats over a 28-day period.** Pharmacology Biochemistry and Behavior. 13(2):215-220, 1980.

After Lister rats at reduced body weight established responding by lever-pressing for nicotine injections under a food delivery schedule for 1 hour daily sessions for 14 days, the rate of responding was maintained over a second 14 day period even if the schedule was removed. Data suggested that rats maintain self-administration of nicotine if the behavior is established for a critical intake of nicotine over a critical period of time. The food delivery schedule facilitated establishment of the behavior, but was not essential for nicotine self-administration in rats. 17 references. (Author abstract modified)

004375 Snyder, E. W.; Shearer, D. E.; Schlehuber, C.; Dustman, R. E.; Beck, E. C. Veterans Administration Medical Center, Neuropsychology Research (151A), Salt Lake City, UT 84148 **Prolonged electrophysiological and behavioral alterations following a single injection of methadone in the cat.** Pharmacology Biochemistry and Behavior. 12(6):893-898, 1980.

Electrophysiological and behavioral alterations following a single injection of methadone in the cat were monitored for 4 days. Most measurements indicated a prolonged drug effect which lasted into the 4th day. Independent alterations of visual evoked potential (VEP) component amplitudes suggest site specific variations in the time course of the drug effects. An early component, reflecting activity of classical ascending pathways, was quite resistant to the drug effects immediately following injection. Only after 31 hours was this component significantly attenuated. The amplitude approached predrug values at the time of final measurement. A late VEP component was quickly suppressed following methadone and returned to predrug values after 55 hours. Decreases in EEG frequency, on the other hand, evidenced no time dependency following drug administration. All animals were behaviorally normal after 55 hours with no further evidence of mania. Results confirm the prolonged effects of methadone in a species known for its unusual and complex response to opiates. Sites within the visual system are apparently highly sensitive to the drug and are differentially altered over time following methadone injection. These alterations are, for the most part, correlated with plasma methadone concentration. 22 references. (Author abstract modified)

004376 Sovilla, Jean-Yves; Magistretti, Pierre; Schorderet, Michel. Schorderet: Dept. de Pharmacologie, Ecole de Medicine, CH-1211 Geneva 4, Switzerland **Potentiation of apomorphine-induced climbing behaviour in mice by d-LSD.** Progress in Neuro-Psychopharmacology. 3(5/6):503-511, 1979.

The potentiation of apomorphine-induced climbing behavior in mice by d-LSD was examined. Doses of d-LSD ranging from 0.25 to 2.5mg/kg injected intraperitoneally constantly inhibited the climbing behavior. In contrast, when similar doses of d-LSD were injected 10 minutes before apomorphine (5mg/kg), a constant potentiation of the apomorphine-induced climbing was observed. Subsequent experiments performed with a neuroleptic (haloperidol) or a serotonin precursor (5-OH-tryptophan) compared to those of d-LSD with and without apomorphine would indicate that d-LSD alone displays typical serotonergic syndrome (including inhibition of the climbing), whereas in the presence of apomorphine, an interaction at presynaptic receptors may possibly modulate dopaminergic activity. 26 references. (Author abstract modified)

004377 Spreux-Varoquaux, Odile; Simon, Pierre. Simon: Dept. de Pharmacologie, Faculte de Medecine Pitie-Salpetriere 91, Boulevard de l'Hopital, F-75634 Paris Cedex 13, France **Interactions between ethanol and amphetamine in mice and rats.** Progress in Neuro-Psychopharmacology. 4(1):13-18, 1980.

Interactions between ethanol and amphetamine were studied on four different psychopharmacological tests. Toxicity of d-amphetamine in aggregated mice was reduced or eliminated by ethanol. Hyperthermia and hypermotility produced by d-amphetamine in mice were partly suppressed by ethanol. Stereotyped behavior produced by d-amphetamine in rats was unchanged after ethanol administration. These effects were observed with acute doses of ethanol given orally. 23 references. (Author abstract modified)

004378 Standish, L. J.; Feldman, R. S. Dept. of Psychology, Smith College, Northampton, MA 01063 **Differential effects of chlordiazepoxide on conditioned and unconditioned behavior in mice with septal lesions.** Psychopharmacology. 61(3):293-297, 1979.

The time course of action of repeated daily doses of chlordiazepoxide (CDP) on conditioned and unconditioned behavior was examined in mice with septal lesions. Bilateral septal lesions produced changes in both conditioned and unconditioned behavior. These lesions increased rate of operant responding on a VI-40 schedule I and produced hyperreactivity to tactile stimuli. The effects of repeated administration of CDP on these two classes of behavior were observed to follow different time courses. In a dose dependent fashion, CDP first reduced VI response rates in septal mice, but after several daily doses the response rate increased above postsurgical baseline levels. The suppressant effects of CDP on septal hyperreactivity were quite different. Hyperreactivity was persistently attenuated by all CDP doses tested during the 8 day drug regimen. The pattern of drug effects suggested that serotonin antagonism is involved in CDP's effects on lesion produced hyperreactivity. 18 references. (Author abstract modified)

004379 Stanley, Michael; Rotrosen, John; Sculerati, Nancy; Gershon, Samuel; Kuhn, Cynthia; Cohen, Bruce M. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Atypical antidopaminergic properties of CI-686: a potential antipsychotic agent.** Psychopharmacology. 66(1):23-27, 1979.

The effects of the antipsychotic/antidepressant drug CI-686 on apomorphine and amphetamine-induced sterotypies, dopamine metabolism, neuroleptic binding, and serum prolactin levels were examined in rats. CI-686 displayed profiles of activity in each of these systems that differ markedly from those of other antipsychotics. CI-686 has a unique clinical profile which suggests a mechanism of action other than dopamine antagonism. The profile of antipsychotic efficacy without extrapryramidal symptoms fails to support the dopamine hypothesis of schizophrenia and has important implications for the pathophysiology of schizophrenia. 24 references. (Author abstract modified)

004380 Syme, G. J.; Syme, L. A. Syme, L. A.: Dept. of Pharmacology, Queen Elizabeth II Medical Centre, University of Western Australia, Nedlands, W. A. 6009, Australia **Inhibition of**

activity in rats by rubidium chloride. Psychopharmacology. 61(2):227-229, 1979.

The effects of two dosages of rubidium chloride on exploration, locomotion, rearing, and immobility were assessed for male and female rats in an exploration box and an open field. In contrast to previous findings, rubidium was found to decrease locomotion and rearing in the exploratory box, and also to decrease locomotion in the open field. Further research in a variety of experimental settings is required before the effects of rubidium on activity can be fully evaluated. 6 references. (Author abstract)

004381 Thiebot, M. H.; Jobert, A.; Soubrie, P. Unite de Recherches de l'Inserm, 2 rue d'Alesia, F-75014 Paris, France **Chlordiazepoxide and GABA injected into raphe dorsalis release the conditioned behavioural suppression induced in rats by a conflict procedure without nociceptive component.** Neuropharmacology. 19(7):633-641, 1980.

A conflict procedure was used to study the effects of chlordiazepoxide (CDP) or diazepam (DZP) on conditioned behavioral suppression in male Wistar rats. Lever-pressing was suppressed by presentation of a signal (lights off) previously paired with punishment. Intraperitoneal injections of DZP or CDP significantly reduced this behavioral suppression without increasing responses to a signal (lights on) previously associated with reward. Muscimol had no direct effect on responding and did not potentiate the disinhibitory effects of DZP. Application of CDP or GABA to the nucleus raphe dorsalis increased lever-pressing during the lights off signal without altering responding during the lights on signal. GABA failed to potentiate the disinhibitory effects of CDP. 40 references. (Author abstract modified)

004382 Tikal, K. Pharmacological Dept., Faculty of Hygiene, Srobarova 50, 100 34 Prague 10, Czechoslovakia **No effect of aminophylline on operant alimentary behaviour of rats.** Activitas Nervosa Superior. 22(1):70-71, 1980.

The effects of aminophylline (theophylline ethylendiamine) on operant alimentary behaviors of rats were investigated. Results indicate that in contrast to most stimulating compounds, aminophylline has no facilitating effect on operant alimentary behavior. These results indicate that the metabolic effects of theophylline (i.e. competitive inhibition of phosphodiesterase which inactivates 3',5'-AMP) play a negligible part in the mechanisms of CNS activation. Some complexities of the role of cyclic 3',5'-AMP are noted. 5 references.

004383 Tikal, K.; Hvizdosova, J.; Pavlovicova, E. Pharmacological Dept., Faculty of Hygiene, Srobarova 50, 100 34 Prague 10, Czechoslovakia **Spontaneous motor activity in rats given repeatedly beta-sympatholytics, propranolol and trimepranol.** Activitas Nervosa Superior. 22(1):71-72, 1980.

Spontaneous motor activity in rats chronically treated with propranolol, trimepranol, or saline were compared. Thirty minutes after the morning application of the drug, the animals were put individually into an observation box consisting of a larger and smaller compartment connected by an opening, and for a period of 3 minutes, horizontal and vertical activity, time of complete immobility, and grooming time were monitored. In comparison to propranolol and saline, trimepranol depressed total motor and grooming activity. 3 references.

004384 Tortella, F. C.; Cowan, A.; Adler, M. W. Dept. of Pharmacology, Temple University School of Medicine, Philadelphia, PA 19140 **EEG and behavioral effects of ethylketocyclazocine, morphine and cyclazocine in rats: differential sensitivities towards naloxone.** Neuropharmacology. 19(9):845-850, 1980.

Ethylketocyclazocine (2.5mg/kg i.p.), morphine (10mg/kg), and cyclazocine (2.5mg/kg) each induced high voltage synchrony in the cortical EEG and behavioral stupor in male Sprague-Dawley rats. This initial phase of EEG synchrony and stupor was followed by EEG activation and behavioral arousal in animals given ethylketocyclazocine or morphine; cyclazocine produced intermittent phases of EEG desynchronization and behavioral excitation. Subcutaneous pretreatment with naloxone (0.01 to 10mg/kg) caused a dose related antagonism of the duration of EEG synchrony and stupor produced by the three analgesics; ethylketocyclazocine was the most sensitive to naloxone and cyclazocine the least sensitive. 28 references. (Author abstract modified)

004385 Tortella, Frank C.; Moreton, J. Edward. Moreton: Dept. of Pharmacology and Toxicology, University of Maryland School of Pharmacy, Baltimore, MD 21201 **D-Ala2-methionine-enkephalinamide self-administration in the morphine-dependent rat.** Psychopharmacology. 69(2):143-147, 1980.

The self-administration of D-enkephalin was studied in the dependent rat self-administering morphine. The rats were prepared with chronic IV and bilateral intraventricular (IVT) injection cannulae. They were made physically dependent on morphine and trained level press for IV morphine self-injections on a fixed ratio 20 schedule of reinforcement. Substitution of D-enkephalin either IVT or IV in the morphine dependent rat maintained consistent lever pressing and self-administration behavior similar to morphine self-administration. No signs of abstinence were observed during the D-enkephalin substitution. However, saline substitution for morphine in the self-administering rat produced an abstinence syndrome characterized by extinction of responding, wet dog shakes, writhes, and diarrhea, which were reversed for 1 h by a single IVT injection of D-enkephalin. These results indicate that D-enkephalin will serve as a reinforcer to maintain opiate seeking behavior and support physical dependence in the rat. 30 references. (Author abstract modified)

004386 Tricklebank, M. D.; Drewitt, P. N.; Curzon, G. Dept. of Neurochemistry, Institute of Neurology, 33 John's Mews, London, WC1N 2NS England **The effect of L-tryptophan on motor activity and its prevention by an extracerebral decarboxylase inhibitor and by 5-HT receptor blockers.** Psychopharmacology. 69(2):173-177, 1980.

L-tryptophan at moderately low dosage reduced the activity of rats taken during a dark period (red light) and put into an open field illuminated by bright white light. Activity was not altered when the field was illuminated by red light. Tryptophan did not cause significant hypoactivity in rats pretreated with the 5-hydroxytryptamine (5-HT) receptor antagonists methysergide, cyproheptadine and metergoline. However, tryptophan did not alter brain 5-HT concentration and only increased 5-hydroxyindoleacetic acid (5-HIAA) slightly in rats killed shortly after behavioral observation. A further indication that the behavioral effect of tryptophan was not due to increased brain 5-HT was its prevention by R04-4602 at a dose sufficient to block peripheral but not central L-aromatic amino acid decarboxylase. Results suggest that the above behavioral effect of L-tryptophan is peripherally mediated. A number of potential mechanisms are discussed. 41 references. (Author abstract)

004387 Tsoucaris-Kupfer, Danita; Liblau, Lola; Legrand, Monique; Schmitt, Henri. Laboratorie de Pharmacologie, Faculte de Medecine, 15 rue de l'Ecole-de-Medecine, F-75270 Paris Cedex 06, France **Central cardiovascular actions of d-tubocurarine and**

inhibition of the hypotensive effect of clonidine. European Journal of Pharmacology. 65(2/3):301-304, 1980.

Intracisternal administration of d-tubocurarine (0.025 to 0.100mg/kg) in dogs anesthetized with alpha-chloralose caused a dose related increase in blood pressure associated with seizures. D-tubocurarine elicited a similar response in dogs pretreated with guanethidine (15mg/kg iv), but bilateral adrenalectomy abolished the pressor response to d-tubocurarine. Pretreatment with d-tubocurarine reversed the hypotensive effect of clonidine (0.003 mg/kg), suggesting the drugs may interact at central GABAergic, glycinergic, of cholinergic synapses. 12 references. (Author abstract modified)

004388 Tyler, Thomas D.; Tessel, Richard E. Tessel: Dept. of Pharmacology and Toxicology, School of Pharmacy, University of Kansas, Lawrence, KS 66045 **Amphetamine's locomotor-stimulant and norepinephrine-releasing effects: evidence for selective antagonism by nisoxetine.** Psychopharmacology. 64(3):291-296, 1979.

A new procedure that allows simultaneous and objective measurement of both locomotor activity and stereotypy in individual mice was used to determine the effects of the selective noradrenergic uptake inhibitor, nisoxetine (Lilly 94939), on amphetamine-induced changes in these behaviors. Amphetamine markedly increased locomotor activity at a dose of 3mg/kg, while sterestypy was significantly increased at doses of 5.6mg/kg and above. After nisoxetine 20mg/kg, 30 minutes pretreatment), the locomotor stimulant effect of amphetamine was abolished and its actions on stereotypy were potentiated. The action of nisoxetine was selective in that it did not significantly affect the locomotor activity induced by a moderate dose of morphine. In addition, nisoxetine pretreatment had little effect on the accumulation of 3H-amphetamine in the mouse brain. Biochemically, nisoxetine antagonized amphetamine-induced release of 3H-norepinephrine from the mouse cerebral cortex, but not that of 3H-dopamine or 3H-5-hydroxytryptamine from the mouse corpus striatum. The data indicate that nisoxetine selectively antagonized certain of amphetamine's behavioral and biochemical actions. They are also consistent with the suggestion that amphetamine-induced release of norepinephrine is causally related to the locomotor stimulant action of amphetamine and may inhibit stereotypy produced by the drug. 38 references. (Author abstract modified)

004389 Ulku, E.; Ayhan, I. H.; Tulunay, F. C.; Uran, B.; Kaymakcalan, S. Ayhan: Dept. of Pharmacology, Ankara University Medical School, Sihhiye, Ankara, Turkey **Effect of delta9-tetrahydrocannabinol on the morphine-induced hyperactivity of mice.** Psychopharmacology. 69(2):201-205, 1980.

The effect of delta-9-tetrahydrocannabinol (THC) on the locomotor activity stimulating action of morphine was investigated in mice. THC was found to potentiate morphine-induced hyperactivity. On the other hand, the stimulating action of morphine on motor activity strongly diminished in mice rendered tolerant by the implanatation of a morphine pellet. The pretreatment of morphine tolerant mice with the same dose of THC did not change the effect of morphine on the motor activitiy. These results suggest that tolerance also developed to the potentiating action of THC on morphine-induced hyperactivity during the development of tolerance to this action of morphine. 20 references. (Author abstract modified)

004390 Van Wagoner, Steven; Risser, Judith; Moyer, Marcia; Lasky, David. Lasky: Dept. of Psychology, Lebanon Valley College, Annville, PA 17003 **Effect of maternally administered methadone on discrimination learning of rat offspring.** Perceptual and Motor Skills. 50(3, Part 2):1119-1124, 1980.

The effects of maternally administered methadone on shape discrimination learning were examined with the 150-day-old offspring of Sprague-Dawley rats. The mothers had been on one of four schedules: prenatal and postnatal methadone, prenatal methadone and postnatal saline, prenatal saline and postnatal methadone, and prenatal and postnatal saline. The prenatal methadone group and the postnatal methadone group showed a deficit in learning when compared to the saline control group. Findings suggest that methadone addiction of the mother can have important behavioral effects even for adult offspring. 19 references. (Author abstract modified)

004391 Watanabe, Hiroshi; Watanabe, Kazuo. Dept. of Pharmacometrics, Research Institute for Wakan-yaku, Toyama University, Toyama 930, Japan **Enhancement of apomorphine-induced rotational behaviour in rats following the combination of 6-hydroxydopamine and electrolytic lesions in the substantia nigra.** Japanese Journal of Pharmacology. 29(1):93-104, 1979.

Drug-induced rotational behavior was studied in Wistar and Donryu rats following electrolytic and 6-hydroxydopamine (6-OHDA) lesions of the substantia nigra (SN). In rats with 6-OHDA lesions of the right SN, apomorphine produced turning toward the left and methamphetamine turning toward the right. Both drugs produced rotations ipsilateral to the lesioned side in rats with unilateral electrolytic SN lesions. When the electrolytic lesion was placed in the right SN after treatment with 6-OHDA, apomorphine-induced rotation toward the left was markedly suppressed but methamphetamine-induced rotation was not altered. When the electrolytic lesion was placed in the left SN of rats with 6-OHDA lesions of the right SN, apomorphine-induced rotation was decreased. The enhanced apomorphine-induced rotation in this group may reflect dysfunction of the postsynaptic factors in the left SN in combination with the denervation supersensitivity to apomorphine in the right SN. 34 references. (Author abstract modified)

004392 Waters, D. H.; Walczak, D. Dept. of Biochemical Pharmacology, School of Pharmacy, State University of New York, Buffalo, NY 14260 **Cholinergic and dopaminergic involvement in phenobarbital-induced locomotor activity in mice.** Neuropharmacology. 19(6):543-547, 1980.

Subhypnotic doses of phenobarbital were found to produce dose related (20 to 80mg/kg) increases in locomotor activity in mice. The phenobarbital-induced locomotor activity was additive with the locomotor activity induced by the anticholinergic agent scopolamine. Haloperidol and alpha-methyl-p-tyrosine completely blocked the phenobarbital-induced increase in locomotor activity. It appears that phenobarbital-induced locomotor activity may result from activation of central dopaminergic pathways secondary to depression of central cholinergic pathways. 26 references. (Author abstract modified)

004393 Weight, M. L.; Ridley, R. M.; Baker, H. F. Ridley: Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, HA1 3UJ, Middlesex, England **The effect of amphetamine on delayed response performance in the monkey.** Pharmacology Biochemistry and Behavior. 12(6):861-864, 1980.

The effect of amphetamine on discrete trial, visual discrimination where response was permitted simultaneously with stimulus presentations or 0, 1, or 3 sec after stimulus presentation, was assessed in the marmoset. An interaction between dose and delay was observed comprising significantly impaired performance after amphetamine under conditions of longer delay. Results are interpreted in terms of loss of response inhibition and increased distraction and are compared with frontal lobe function in the primate. Similarities between the effects of amphet-

amines and frontal ablations are discussed. 16 references. (Author abstract modified)

004394 Weinstock, Marta; Weiss, Carmella. Dept. of Pharmacology and Experimental Therapeutics, Hebrew University, Hadassah Medical School, Jerusalem, Israel **Antagonism by propranolol of isolation-induced aggression in mice: correlation with 5-hydroxytryptamine receptor blockade.** Neuropharmacology. 19(7):653-656, 1980.

The aggression induced in male Sabra mice by prolonged isolation was prevented by beta-adrenoceptor antagonists and serotonin (5-HT) receptor antagonists in doses similar to those required to antagonize head twitches induced by 5-hydroxytryptophan (5-HTP). Methysergide, cyproheptidine, K()-propranolol, and pindolol all reduced isolation-induced fighting in doses of 0.5 to 4.0mg/kg. Metroprolol, atenolol, and ()-propranolol were inactive. A 10mg/kg dose of 5-HTP increased aggressive behavior in isolated mice. Results suggest that fighting behavior is associated with activation of central 5-HTP pathways and that beta-adrenoceptor antagonists prevent this behavior by blocking 5-HT receptors. 14 references. (Author abstract modified)

004395 Weischer, Marie-Luise. Inst. f. Pharmakologie und Toxikologie der Universitat, Westring 12, D-4400 Munster, Germany **/Influence of lithium and rubidium on exploratory behavior and locomotor activity in isolated male mice./** Einfluss von Lithium und Rubidium auf Neugierverhalten und lokomotorische Aktivitat isoliert gehaltener mannlicher Mause. Psychopharmacology. 61(3):263-266, 1979.

The effect of lithium and rubidium on curiosity rearing, and locomotor activity in isolated and group housed male mice (DBA/2 Han) was investigated. LiCl and RbCl were given with the drinking water (30mol/l) during 3 weeks. The behavior of the animals was tested before and after the chronic application of either lithium or rubidium. Results show that lithium enhanced the decreased curiosity of the isolated mice, bringing it to levels which were not significantly different form those of group housed animals. Locomotor activity of isolated animals was also increased by LiCl, while rearing was not altered. Rubidium greatly decreased the already diminished curiosity of the fighting mice but had no influence on rearing and locomotor activity. Three weeks after cessation of treatment, the behavior of the isolated mice returned to predrug levels. Neither lithium nor rubidium had any influence on the behavior of group housed animals. 27 references. (Author abstract modified)

004396 Wenger, Galen R. Dept. of Pharmacology, University of Arkansas for Medical Sciences, Little Rock, AR 72205 **Effects of phencyclidine and ketamine in pigeons on behavior suppressed by brief electrical shocks.** Pharmacology Biochemistry and Behavior. 12(6):865-870, 1980.

The effects of phencyclidine and ketamine in pigeons on behavior suppressed by brief electrical shocks were investigated and compared with the effects of pentobarbital, d-amphetamine, and morphine. Phencyclidine and ketamine, over a narrow dose range, produced small increases in responding under the FR 30 (shock) component of both mixed and multiple schedules. By comparison, pentobarbital produced very large increases in responding under the FR 30 (shock) component of both schedules. Increasing doses of d-amphetamine and morphine either had no effect on, or decreased the response rate in both components of the mixed and multiple schedules. Results suggest that phencyclidine and ketamine may have some properties qualitatively like pentobarbital and unlike d-amphetamine and morphine in attenuating the suppression of behavior produced by brief electrical shocks. 33 references. (Author abstract modified)

004397 Wishart, T. B.; Herberg, L. J. Herberg: Institute of Neurology, National Hospital for Nervous Diseases, Queen Square, London WC1N 3BG, England **Central cholinergic mechanisms in electrical self-stimulation and in drug-induced tremor in rats.** Pharmacology Biochemistry and Behavior. 11(6):625-629, 1979.

Central cholinergic mechanisms in electrical self-stimulation and in drug-induced tremor in rats were investigated. Oxotremorine, a specific stimulant of central muscarinic acetylcholine receptors, inhibited lateral hypothalamic self-stimulation at a dose level less than one tenth of that necessary to produce body tremor. Tremor induced by oxotremorine (0.5mg/kg) was inhibited by pretreatment with hyoscine (scopolamine) or propranolol but not by methylhyoscine or apomorphine. Inhibition of self-stimulation by oxotremorine was prevented by hyoscine but not by any other of the drugs tested and thus constitutes a uniquely specific in vivo model for assessing central antimuscarinic activity. Results confirm the presence of centrally situated ACh receptors eliciting tremor and inhibiting self-stimulation but provide no evidence of an effect on tremor by central adrenergic beta-receptors. 23 references. (Author abstract modified)

004398 Wolf, Michael D.; Wilcox, Richard E.; Riffee, William H.; Abraham, Lawrence D. Wilcox: Dept. of Pharmacology, College of Pharmacy, University of Texas, Austin, TX 78712 **Strain differences in dopamine receptor function and the initiation of movement.** Pharmacology Biochemistry and Behavior. 13(1):5-7, 1980.

Voluntary movement initiation (VMI) and caudate nucleus dopamine receptor binding were studied in Charles River CD/F-344 (CR-CD/F) and Zivic-Miller CD (ZM-CD) rats. Although 86% of the CR-CD/F rats were trained to rapidly release and reset a response lever to avoid electric shock, only 43% of the ZM-CD rats completed training. Among rats that completed training, the CR-CD/F rats showed marginally higher avoidance percentages and significantly faster VMI latencies. Binding affinity for (3H) spiroperidol was significantly higher in striatal homogenates from trained CR-CD/F rats than from trained or untrained ZM-CD rats. The maximum density of dopamine receptors was signficantly higher in trained ZM-CD rats than in ZM-CD rats that could not be trained or in trained CR-CD/F rats. 11 references. (Author abstract modified)

004399 Wolff, Dieter L.; Zeller, H.-J.; Zschenderlein, R.; Hinz, G. Central Inst. Occup. Medicine, Noldnerstrasse 40-42, DDR-1134 Berlin, Germany **Behavioural, electroneurographical, and histological investigations in rats concerning the combined action of styrene and ethanol.** Activitas Nervosa Superior. 21(4):260-261, 1979.

Behavioral, electroneurographical, and histological investigations of the combined action of styrene and ethanol in rats are presented. Ethanol, styrene, or ethanol plus styrene were administered by stomach tube for 4 weeks, 5 days/week, to male Wistar rats. Ethanol alone did not change the hole board reaction, orienting reflex, or open-field behavior, but styrene alone decreased the number of orienting reflexes, the number of hole board reactions, and the number of entered squares in the open field. The combination of alcohol and styrene resulted in potentiation of styrene effects on orienting reflexes and open-field activity, but not one hole board reaction. It is concluded that: 1) ethanol alone exhibits no behavioral effects, but is more toxic than styrene on the peripheral nervous system; and 2) styrene alone affects all behavioral tests, influences preferentially the slow conducting peripheral nervous fibers, and causes a mild selective damage of the Purkinje cells. 8 references.

004400 Yamada, Katsushi; Furukawa, Tatsuo. Dept. of Pharmacology, School of Medicine, Fukuoka University, Fukuoka 814, Japan **Serotonergic function in mouse head twitches induced by lithium and reserpine.** Psychopharmacology. 61(3):255-260, 1979.

Serotonergic function in mouse head twitches induced by the combination of lithium and reserpine was investigated. Head twitches were elicited by combined treatment with lithium chloride and rauwolfia alkaloids, i.e., reserpine, tetrabenazine, and syrosingopine. Neither lithium nor the alkaloid alone induced the twitches; nor did combined administration of lithium with methamphetamine or p-chloroamphetamine. The head twitches induced by lithium in combination with reserpine were strongly inhibited by antiserotonin drugs, methysergide and cyproheptadine, and also by a serotonin synthesis inhibitor, p-chlorphenylalanine (PCPA), when administered between lithium and reserpine. When PCPA was administered before lithium for 3 days, the head twitches were potentiated. In addition, the head twitches were potentiated by a serotonin receptor stimulant, 5-methoxy-N,N-dimethyltryptamine. Results imply that lithium can induce head twitches in the presence of rauwolfia alkaloids and may exert its effect in part by acting on the serotonergic neuron system. 37 references. (Author abstract modified)

004401 Young, Alice M.; Thompson, Travis. Thompson: Dept. of Psychology, University of Minnesota, Minneapolis, MN 55455 **Naloxone effects on schedule-controlled behavior in morphine-pelleted rats.** Psychopharmacology. 62(3):307-314, 1979.

The effects of morphine pellet implantation and naloxone administration were examined in rats lever-pressing under interresponse time schedules of food presentation. Subcutaneous implantation of a morphine pellet initially decreased lever-pressing rates. Tolerance to this effect developed within 3 to 4 days. Naloxone decreased response rates in morphine pelleted rats in a dose dependent and time dependent manner. Decreases in response rate were due to an increased frequency of long pauses and not to marked shifts in the temporal patterning of those lever-presses that did occur. Changes in response rate after naloxone were accompanied by bodyweight loss. 28 references. (Author abstract modified)

004402 Young, Gerald A.; Steinfels, George F.; Khazan, Naim. Dept. of Pharmacology and Toxicology, University of Maryland School of Pharmacy, 636 West Lombard St., Baltimore, MD 21201 **Narcotic abstinence in dependent rats: EEG and behavioral correlates.** Pharmacology Biochemistry and Behavior. 13(1):115-119, 1980.

REM sleep was significantly suppressed in dependent female Sprague-Dawley rats withdrawn from morphine, methadone, or nor-1-alpha-acetylmethadol (NLAAM), but not in those withdrawn from 1-alpha-acetylmethadol (LAAM) or dinor-1-alpha-acetylmethadol (DNLAAM). Significant increases in head shake behavior were seen during morphine, NLAMM, and DNLAAM abstinence, but not during LAAM abstinence. Significant increases in lever-pressing for saline emerged more rapidly after withdrawal from morphine, methadone, or NLAMM than during NLAAM or DNLAAM abstinence. 27 references. (Author abstract modified)

004403 Zacharko, Robert M.; Wishart, Thomas B. Psychology Dept. University of Saskatchewan, Saskatoon, Saskatchewan S7N OWO, Canada **Facilitation of self-stimulation with high doses of amphetamine in the rat.** Psychopharmacology. 64(2):247-248, 1979.

Rats were trained to self-stimulate by interrupting a photobeam, and brain stimulation (to the medial forebrain bundle) was maintained for as long as the beam of light was broken. d-Amphetamine sulfate was then administered and response rate and total duration of stimulation were recorded. Both response rate and total duration were elevated by 1, 2, and 5mg/kg doses. The 1.4 sec preferred response duration observed with saline was elevated to 2 sec with 2 and 5mg/kg doses of d-amphetamine. Thus, while animals in a lever-pressing task engage in vigorous stereotypy and seldom or slowly respond to stimulation, in the photobeam task the animal's ability to respond was not seriously impaired by the stereotypy which occurred. Further, results showed that increased responding occurred due to the effects of the rewarding stimulation, and not as a consequence of stereotypy. Results therefore, fail to support Stein and Wise's (1969, 1970) hypothesis that high doses of amphetamine reduce reward value in rats responding for brain stimulation. 5 references. (Author abstract modified)

004404 Zaluzny, S. G.; Chesher, G. B.; Jackson, D. M.; Malor, R. Chesher: Dept. of Pharmacology, University of Sydney, New South Wales 2006, Australia **The attenuation by delta9-tetrahydrocannabinol and morphine of the quasi-morphine withdrawal syndrome in rats.** Psychopharmacology. 61(2):207-216, 1979.

The effect of delta9-tetrahydrocannabinol (THC), morphine, haloperidol, and chlordiazepoxide on the exhibition of the signs of the quasimorphine withdrawal syndrome was studied in rats. In preliminary studies, approximately equisedative doses of these drugs were chosen. Morphine and THC produced a very similar degree of suppression of the signs of the quasimorphine withdrawal, but unlike morphine, the effects of THC were not reversed by the narcotic antagonist, naloxone. The dopamine receptor antagonist, haloperidol, produced a moderate suppression of the withdrawal syndrome and chlordizepoxide was without significant effect. It is concluded that THC is of very similar potency to morphine in suppressing the quasimorphine withdrawal syndrome, but its activity in this regard does not appear to be dependent upon the availability of opiate or dopamine receptors, nor is it due to sedation alone. 24 references. (Author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

004405 Aaseth, Jan; Soli, Nils E.; Forre, Oystein. Institute of Occupational Health, PO Box 8149, Dep., Oslo 1, Norway **Increased brain uptake of copper and zinc in mice caused by diethyldithiocarbamate.** Acta Pharmacologica et Toxicologica. 45(1):41-44, 1979.

Sodium diethyldithiocarbamate (0.5mlmol/kg) was given to female NMRI mice together with radiolabeled copper or zinc to determine the effect of the chelating agent on the distribution of the two elements. Diethyldithiocarbamate increased the brain level of radioactive copper fivefold and that of radioactive zinc threefold. This redistribution of metal ions may have been due to the formation of lipophilic metal chelates. The increased brain levels may be involved in the neurotoxicity reported for diethyldithiocarbamate. 15 references. (Author abstract modified)

004406 Bockhardt, Hans; Lullmann-Rauch, Renate. Dept. of Anatomy, University of Kiel, D-2300 Kiel, Germany **Zimelidine-induced lipidosis in rats.** Acta Pharmacologica et Toxicologica. 47(1):45-48, 1980.

The antidepressant zimelidine induced generalized lipidosis in male Wistar rats. In rats treated chronically with high oral doses (80mg/kg), lipidosis-like cellular alterations were seen in lung, adrenal cortex, and lymphatic tissue. Mild lysosomal alterations were seen in hepatocytes, adrenal medulla, retinal pigment epithelium, and peripheral and central nerve cell perikarya. 7 references. (Author abstract modified)

004407 Christensen, A. V.; Nielsen, I. Moller. Dept. of Pharmacology and Toxicology, H. Lundbeck & Co. A/S, Ottiliavej 7-9, DK-2500, Copenhagen-Valby, Denmark **Dopaminergic supersensitivity: influence of dopamine agonists, cholinergics, anticholinergics, and drugs used for the treatment of tardive dyskinesia.** Psychopharmacology. 62(2):111-116, 1979.

The intensity of dopaminergic supersensitivity of mice after single and repeated administration of neuroleptics was investigated as well as whether or not additional treatment with a dopamine agonist could prevent induction of supersensitivity. It was found that supersenstivity induced by neuroleptics is time dependent and that it can be prevented by additional treatment with DA agonists but not by cholinergic/anticholinergic treatment. In the supersensitivity phase, the syndrome is suppressed by dopamine agonists but enhanced by GABA agonists, benzodiazepine and phenobarbital. 46 references. (Author abstract modified)

004408 Dantzer, Robert. INRA, Station de Pharmacologie-Toxicologie, 180, chemin de Tournefeuille, F-31300 Toulouse, France **Conditioned taste aversion as an index of lead toxicity.** Pharmacology Biochemistry and Behavior. 13(1):133-135, 1980.

Male Wistar rats treated with lead acetate after consuming a solution with a distinct taste subsequently showed an aversion to the initial taste solution. The conditioned taste aversion was reliably induced with 10 to 20mg/kg lead acetate, and repeated lead treatment did not enhance the effect in forced or free choice situations. The use of the taste aversion procedure to evaluate toxicity is discussed. 13 references. (Author abstract modified)

004409 Descotes, J.; Lievre, M.; Ollagnier, M.; Faucon, G.; Evreux, J. C. Laboratory of Pharmacology, Alexis Carrel Medical Faculty, Rue Guillaume Paradin, F-69008 Lyon, France **Study of thioridazine cardiotoxic effects by means of his bundle activity recording.** Acta Pharmacologica et Toxicologica. 44(5):370-376, 1979.

The effects of thioridazine on sinusal automaticity, myocardial excitability, and auriculoventricular conduction were studied in dogs by measuring the spontaneous heartrate, the effective refractory period of the atrial contractile tissue, and the time of auriculonodal and infrahisian conduction. Thioridazine hydrochloride (10mg/kg i.v.) did not alter sinusal automaticity in chloralose anesthetized dogs, but prolonged infrahisian and suprahisian conduction times and increased the atrial refractory period. These effects are related to quinidine-like properties and are consistent with the cardiotoxic effects of phenothiazines reported in clinical practice. 34 references. (Author abstract modified)

004410 Gordon, John H.; Borison, Richard L.; Diamond, Bruce I. Dept. of Pharmacology, Chicago Medical School, 2020 West Ogden Ave., Chicago, IL 60612 **Estrogen in experimental tardive dyskinesia.** Neurology. 30(5):551-554, 1980.

Ovariectomized female Sprague-Dawley rats were treated with haloperidol (0.5mg/kg) alone or combined with estradiol benzoate (EB, 8mcg/kg) for 16 days and challenged with apomorphine (0.25mg/kg) 4 and 10 days after termination of the chronic treatments. Chronic treatment with haloperidol alone enhanced responses to apomorphine, whereas haloperidol combined with EB produced a synergistic response. Apomorphine-induced stereotypy was attenuated in animals treated chronically with haloperidol and then given daily DB. Results suggest that estrogen may mask the development of tardive dyskinesia. 23 references. (Author abstract modified)

004411 Gupta, C.; Sonawane, B. R.; Yaffe, S. J.; Shapiro, B. H. Dept. of Pediatrics, School of Medicine, University of Pennsylvania, Philadelphia, PA 19104 **Phenobarbital exposure in utero: alterations in female reproductive function in rats.** Science. 208(4443):508-510, 1980.

The long-term effects on reproductive function of exposure to phenobarbital in utero were investigated in Sprague-Dawley rats. Phenobarbital administration to pregnant rats from day 12 to day 19 of gestation suppressed body weight gain and produced significant effects on reproductive function in their offspring. These effects included delays in the onset of puberty, disorders in the estrous cycle, and infertility. Moreover, animals exposed to phenobarbital in utero showed altered concentrations of sex steroids, gonadotropic hormones, and estrogen receptors. These findings suggest that phenobarbital treatment during prenatal development can produce permanent alterations in sexual maturation. 22 references. (Author abstract modified)

004412 Kostellow, A. B.; Ziegler, D.; Kunar, J.; Fujimoto, G. I.; Morrill, G. A. Dept. of Physiology, Albert Einstein College of Medicine, 1300 Morris Park Ave., New York, NY 10461 **Effect of cannabinoids on estrous cycle, ovulation and reproductive capacity of female A/J mice.** Pharmacology. 21(1):68-75, 1980.

Treatment with crude marihuana extract (CME) or delta9-tetrahydrocannabinol (THC) in doses approximating light human consumption had no prolonged effect on estrous cycle, mating, or pregnancy in female A/J mice. Doses equivalent to moderate and heavy human use had no long-term effect on estrous cycles or mating, but did show a dose dependent supression of pregnancy. No significant differences were found between the effects of THC and CME containing an equivalent amount of THC. 13 references. (Author abstract modified)

004413 Lehotzky, Kornelia; Szeberenyi, M. Judit. State Institute of Occupational Health, 1450 POB 22, Budapest, Hungary **Central and peripheral neurotoxic action of dimefox in rats.** Activitas Nervosa Superior. 21(4):272-273, 1979.

The central and peripheral neurotoxic action of dimefox in rats was examined. Changes in maze behavior and conditioned avoidance reflex behavior, alternation of the maximal motor conduction velocity (MCV) of the tail nerve of poisoned rats, cholinergic symptoms, and cholinesterase activity of the whole blood and brain were measured following acute and subacute doses over a period of 6 weeks. Subacute doses of dimefox caused long lasting ChE inhibition over the 6 week period. No linear correlation between ChE inhibition, behavioral effects, and dose were found. 4 references.

004414 Mirkova, E.; Hinkova, L.; Vassileva, L; Bogdanova, N. Institute of Hygiene and Occupational Health, D. Nestorov 15, Sofia, Bulgaria **Xylene neurotoxicity in pregnant rats and fetuses.** Activitas Nervosa Superior. 21(4):265-268, 1979.

Xylene neurotoxicity in pregnant rats and fetuses was investigated. Eight pregnant Wistar rats were treated dermally with xylene at doses of 2000, 200, and 100mg/kg throughout the gestation (1st through 20th days). Results indicated that xylene causes dose dependent, brain metabolic disturbances, with decreases in mothers' brain ChE and CytO the most susceptible index of xylene neurotoxicity. Xylene increased the G6PDH activity at the highest dose level and DNA concentration and soluble proteins were reduced at 2000 and 200mg/kg doses. Pregnant females exhibited reduced motor activity and defecation in open field. ChE and CytO activity in fetal brain were inhibited by the higher doses, while MHD, i-CDH, and G6PDH activity were increased. 4 references.

004415 Patsalos, P. N.; Rigor, B. M.; Wiggins, R. C. Wiggins: Neurobiology and Anatomy, University of Texas Medical School at Houston, P.O. Box 20708, Houston, TX 77025 **A halothane-related effect on rat brain myelination: a comparison of chronic prenatal or postnatal exposure.** Journal of Neurochemistry. 35(2):412-416, 1980.

Rats were exposed to 0.5% halothane in air for 8 h/day during the following intervals to assess the halothane effects on rat brain myelination: 1) 5 days postconception to birth; 2) birth to 5 days postnatal age; or 3) birth to 10 days postnatal age. Although prenatal exposure had no effects, 5 days of postnatal exposure caused a 10% reduction in body and brain weight and a 10% relative reduction in the synthesis of brain myelin. The effect persisted throughout the period of rapid postnatal brain myelination. Ten days of postnatal exposure produced equivalent, more severe effects on body and brain weights and a more severe effect of myelin synthesis. Postnatal exposure had no apparent effect on the relative synthesis of nonmyelin particulate proteins. 29 references. (Author abstract modified)

004416 Post, Claes; Andersson, Rolf G. G. Dept. of Clinical Pharmacology, Linkoping University, S-581 85 Linkoping, Sweden **Interactions between lidocaine, norepinephrine and nortriptyline in rat lung slices.** Acta Pharmacologica et Toxicologica. 45(5):403-404, 1979.

The effect of tritiated 1-norepinephrine (3H-NE) in rat lung slices was inhibited by the tricyclic antidepressant nortriptyline (NT). Lidocaine had no effect on 3H-NE uptake when given alone, but significantly increased the uptake of 3H-NE in NT treated preparations. Results suggest that the clinical improvement in symptoms of NT intoxication reported after lidocaine treatment may be due to improved uptake of NE in the ling, and possibly the heart. 6 references.

004417 Szczech, J. Dept. of Neuropathology, AM, Przybyszewskiego 49, 60-355 Poznan, Poland **The activity of phosphatases and esterases in the rat amygdala in the course of experimental intoxication by cynkotox.** Activitas Nervosa Superior. 21(4):281-282, 1979.

The activity of phosphatases and esterases in the rat amygdala in the course of experimental intoxication by cynkotox (zinc diethyldithiocarbamate) was studied. Twenty-two Wistar rats were treated intragastrically with 1.0g of cynkotox in water suspension of 14 days, and their brains were subjected to a morphological and histoenzymatic study. Morphological changes following acute intoxication by cynkotox were vacuolosation, edema and shrinkage of neurons, hypertrophy, and edema of oligodendroglia. Histoenzymatic examination as revealed decreased NsE activity in neurocytes and pericytes. AChE activity was decreased in neurocytes and neuropil, while ATPase activity was weaker in walls of blood vessels and astroglia cells. Results indicate that morphological and enzymatic changes produced by cynkotox are similar to those produced by mercury pesticides. 4 references.

004418 Tabacova, S.; Hinkova, L. Institute of Hygiene and Occupational Health, D. Nestorov 15, Sofia 1431, Bulgaria **Neurotoxicological screening of early effects of prenatal carbon disulfide exposure.** Activitas Nervosa Superior. 21(4):268-269, 1979.

Neurotoxicological screening of early effects of prenatal carbon disulphide (CS2) exposure is described. Pregnant albino rats were exposed to CS2 vapors during gestation, and the 292 pups from 29 litters underwent postpartum screening for onset of reflexes, sensory development, neuromuscular functions, and behavioral development during the first month of life. Postnatal sensory development was significantly retarded in exposed pups, and hyperactivity was observed on days 9 and 14. By day 21, the hyperactivity of the exposed pups had normalized. Decreased learning capacity was observed between day 25 and 30. Thus, CS2 applied in concentrations below those producing congenital malformations provoked neurological and behavioral deficits..2 references.

004419 Tham, R.; Larsby, B.; Odkvist, L. M.; Norlander, B.; Hyden, D.; Aschan, G.; Bertler, A. Dept. of Otolaryngology, Linkoping University, S-58185, Linkoping, Sweden **The influence of trichloroethylene and related drugs on the vestibular system.** Acta Pharmacologica et Toxicologica. 44(5):336-342, 1979.

Following i.v. infusion of trichloroethylene in doses sufficient to produce blood levels above 30ppm, nystagmus induced by positional changes was observed in rabbits. Two metabolites of trichloroethylene, chloral hydrate and trichloroethanol, did not induce nystagmus. Alpha-chloralose, a derivative of chloral hydrate induced positional nystagmus and also markedly exaggerated nystagmus developed during rotatory acceleration. It is suggested that industrial solvents like trichloroethylene cause visual disturbances by stimulating central subcortical vestibular/oculomotor connections. This stimulation may be due to a blockade of inhibitory systems. 19 references. (Author abstract modified)

004420 Thams, Peter; Geisler, Arne. Dept. of Pharmacology, University of Copenhagen, 20, Juliane Maries Vej, DK-2100 Copenhagen 0, Denmark **Dissociation by lithium of hormone-induced formation of cyclic AMP and release of glycerol in isolated rat fat cells.** Acta Pharmacologica et Toxicologica. 46(5):382-387, 1980.

Lithium inhibited the norepinephrine (NE)-induced accumulation of cyclic AMP and release of glycerol in isolated Wistar rat fat cells, but only in the lower dose range for NE. At maximally effective NE concentrations, lithium inhibited the NE-induced cyclic AMP accumulation, but did not affect lipolysis. Basal cyclic AMP content and basal release of glycerol were not altered by lithium. Lithium was also able to stimulate glycerol release by feedback inhibition of free fatty acids of adenylate cyclase or triglyceride lipase. 19 references. (Author abstract modified)

004421 Vendsborg, Per B. Psychochemistry Institute, University of Copenhagen, Rigshospitalet, DK-2100 Copenhagen, Denmark **Weight gain and body composition in lithium treated rats.** Acta Pharmacologica et Toxicologica. 46(5):373-381, 1980.

Female Wistar rats treated chronically with lithium (0.8 to 2.0mmol/kg/day) gained weight significantly faster than control animals. Body composition was not altered. Stomach, large intestine, and small intestine weights were increased. 47 references. (Author abstract modified)

004422 Vocci, Frank J.; Rhody, Jeffrey M.; London, Edythe D.; Buterbaugh, Gary G. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Regional brain 3H-digitoxigen in and monoamine content during the development of convulsions produced by system digitoxigenin.** Research Communications in Chemical Pathology and Pharmacology. 29(2):251-263, 1980.

When 3H-digitoxigenin (3H-DIGT) was given by i.v. infusion to conscious male Sprague-Dawley rats, behavioral and motor disturbances developed as 3H-DIGT uptake increased in the medulla-pons, cerebellum, cerebral cortex, corpus striatum, hippocampus, hypothalamus, and midbrain. After 4 minutes of infusion, during clonic convulsions, uptake appeared to follow reported differences in regional blood flow. Electroshock convulsions after 2 minutes of infusion double or tripled 3H-DIGT

uptake in all regions. No significant monoamine alterations were observed, with the exception of a slight decrease in serotonin level in the medulla-pons after 5.5 minutes of infusion. 27 references. (Author abstract modified)

004423 Wagner, G. C.; Ricaurte, G. A.; Johanson, C. E.; Schuster, C. R.; Seiden, L. S. Dept. of Biopsychology, University of Chicago, 5848 South University Ave., Chicago, IL 60637 **Amphetamine induces depletion of dopamine and loss of dopamine uptake sites in caudate.** Neurology. 30(5):547-550, 1980.

Long lasting depletion of dopamine and cocomitant loss of dopamine uptake sites were observed in male Sprague-Dawley rats after repeated treatment with d-amphetamine, but not after treatment with methylphenidate. Methylphenidate also failed to produce long-term depletion of regional catecholamines in rhesus monkeys. Results indicate that amphetamine has toxic interactions with dopaminergic neurons, which do not occur with methylphenidate. 14 references. (Author abstract modified)

004424 Winneke, G. Medizinisches Inst. f. Lufthygiene und Silikoseforschung, Universitat Duseldorf, Gurlittstr. 53, D-4 Dusseldorf, Germany **Modification of visual evoked potentials in rats after long-term blood lead elevation.** Activitas Nervosa Superior. 21(4):282-284, 1979.

The modification of visual evoked potentials in rats following chronic blood lead elevation was investigated. Visual cortex responses of adult rats that had been exposed prenatally and/or postnatally to different lead concentration in their diets were compared. Data support findings of lead-induced damage to the visual system at higher exposure levels, but suggest that damage threshold exists between 30 and 40mcg/dl in rats. Findings of lead-induced deficits in visual discrimination learning in rats at levels around 30 mcg/dl cannot be explained on the basis of lead-induced damage to the visual system. Latency data are compared to those of Fox et al. (1977). 4 references.

004425 Young, Robert Wilson. Catholic University of America **Prediction of the relative toxicity of environmental toxins as a function of behavioral and non-behavioral endpoints. (Ph.D. dissertation).** Dissertation Abstracts International. 40(4):1937-B, 1979. Ann Arbor, Univ. Microfilms No. 7921632, 122p., 1979.

The differential effects of behavioral and nonbehavioral endpoints on the prediction of the relative toxicity of an environmental toxin were examined. Forty rhesus monkeys were irradiated in groups of four at five different dose levels of high energy neutron and Bremsstrahlung radiations. It was found that behavioral indices were more sensitive to gamma radiation than physiological indices, and that physiological indices were more sensitive to neutron radiations than behavioral indices. The results are interpreted as evidence that behavioral measures can be uniquely sensitive to certain toxins. Based on the similarities between radiation-induced behavioral changes and behavioral changes induced by chemicals which damage the central nervous system via anoxia, it is concluded that the radiation-induced behavioral changes resulted from anoxia. Methodological implications are discussed. (Journal abstract modified)

004426 Zetler, Gerhard. Institut fur Pharmakologie, Medizinische Hochschule Lubeck, Ratzeburger Allee 160, D-2400 Lubeck, Germany **Anticonvulsant effects of caerulein and cholecystokinin octapeptide, compared with those of diazepam.** European Journal of Pharmacology. 65(2/3):297-300, 1980.

Subcutaneous injection of caerulein or the C-terminal octapeptide of cholecystokinin (CCK-8) in male NMRI mice delayed the onset and retarded the development of toxic effects of convulsants such as strychnine, pentetrazol, bicuculline, and picrotoxin. Both peptides were at least as potent as diazepam in increasing the seizure threshold doses of iv pentetrazol and picrotoxin. The anticonvulsive properties of these neuropeptides suggests that convulsive disorders may arise from an abnormal function of CCK-like peptides in the brain. 11 references. (Author abstract modified)

06 METHODS DEVELOPMENT

004427 Bizzini, B.; Grob, P.; Glicksman, M. A.; Akert, K. Akert: Brain Research Institute, University of Zurich, CH-8029 Zurich, Switzerland **Use of the B-IIb tetanus toxin derived fragment as a specific neuropharmacological transport agent.** Brain Research. 193(1):221-227, 1980.

When the Ibc tetanus toxin fragment was coupled to the B-IIb fragment by a disulfide bond, it was transported retrogradely from axonal endings in muscle to the motoneuronal perikarya in female Sprague-Dawley rats. In contrast, the Ibc fragment alone was not transported. It is suggested that fragments like B-IIb serve as specific carriers into the CNS for chemical and chemotherapeutic agents. 19 references. (Author abstract modified)

004428 Cohen, B. M.; Herschel, M.; Miller, Edith; Mayberg, Helen; Baldessarini, R. J. Dept. of Psychiatry, Harvard Medical School, Boston, MA 02115 **Radioreceptor assay of haloperidol tissue levels in the rat.** Neuropharmacology. 19(7):663-668, 1980.

A simple and reliable radioreceptor assay (RRA) was used to measure haloperidol levels in male Sprague-Dawley rat serum and brain. The RRA, which involves competition for 3H-spiroperidol binding to a membrane preparation of calf caudate nucleus, was able to measure haloperidol sensitively to 3pmol/ml serum and 140pmol/g brain. Recovery of haloperidol from serum or brain was 90 to 100%. Excellent correlations were found among results obtained with the RRA, gas chromatography/mass spectrometry, and radioimmunoassay. 21 references. (Author abstract modified)

004429 Corrigall, William A.; Lucato, Rosemarie. Neurobiology Section, Addiction Research Foundation, 33 Russell St., Toronto, Ontario, M5S 2S1, Canada **A simple modification to permit fast-flow perfusion of brain slices.** Brain Research Bulletin. 5(4):481-482, 1980.

A standard tissue slice chamber was modified to permit stabilization of brain slices during rapid perfusion. Opiate effects on field potential responses in rat hippocampal slices were similar in experiments using the tradition slow perfusion (2ml/minute) with a single support net or fast perfusion (7 to 10ml/minute) with a double net assembly modification. Baseline responses stabilized more quickly in transverse hippocampal slices maintained in the double net assembly. 9 references. (Author abstract modified)

004430 Goudie, A. J. Psychology Dept., Liverpool University, P. O. Box 147, Liverpool, L69 3BX, England **Aversive stimulus properties of drugs.** Neuropharmacology. 18(12):971-979, 1979.

The use of the conditioned taste aversion (CTA) procedure to evaluate the aversive stimulus properties of drugs is discussed. Studies that implicate central emetic systems in the acquisition and recall of CTA induced by self-administration of drugs has been described as paradoxical, since some drugs induce CTA at the same doses that maintain self-administration. It is concluded that data obtained with the CTA procedure cannot be properly interpreted until several fundamental questions about the procedure have been answered. 83 references. (Author abstract modified)

004431 Knipe, Jay O.; Coward, James K. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT

06510 **Role of buffers in a methylase model reaction. General base catalysis by oxyanions vs. nucleophilic dealkylation by amines.** Journal of the American Chemical Society. 101(15):4339-4348, 1979.

The role of buffers in a methylase model reaction was examined, and general base catalysis by oxyanions was compared with general base catalysis via nucleophilic dealkylation by amines. The cis-cyclopentanol derivative, (I), was synthesized as a model for the O-methylation of ribose of tRNA, as catalyzed by tRNA 2'-0-methyltransferase. The decomposition of I in oxyanion buffers was studied over a wide pH range, at 25 degrees and 40 degrees C. This reaction exhibits a plateau rate at low pH (kROH) and a hydroxide dependence at higher pH, associated with kRO-. Data indicate that I cyclizes in an intramolecular fashion to give cis-2-oxabicyclo(3.3.0)octane (III) and p-nitrothioanisole (XII) in a reaction which is catalyzed by the added buffer base. The fact that the transanalogue, II which cannot undergo intramolecular alkylation, is inert in oxyanion buffers rules out any participation by buffer base in an intermolecular reaction. When the reaction of I is carried out in amine buffers, however, both p-nitrothionanisole and (2-cis-hydroxycyclopentyl)ethyl p-nitorophenyl sulfide (IV) are detected in the reaction mixture by high pressure liquid chromatographic (LC) analysis. Data indicate that amine buffers preferentially effect nucleophilic demethylation rather than function as general base catalysts, as do the oxyanions. No nucleophilic catalysis by imidazole of the demethylation of I, II, or dimethyl-p-nitrophenylsulfonium perchlorate could be demonstrated. 39 references. (Author abstract modified)

004432 Kovac, L.; Peterajova, El.; Pogady, J. Institute of Animal Physiology, Slovak Academy of Sciences, 900 28 Ivanka pri Dunaji, Czechoslovakia **Drosophila melanogaster, a new subject in research on behaviour and in pharmacology.** Agressologie. 20(D):239-244, 1979.

The possibility of using the fruit fly Drosophila melanogaster as a new experimental animal in research on behavior and its pharmacological modification is explored. The ethogram of Drosophila behavior outlined and several procedures to follow is/ when studying locomotor and sexual activities are described. Reserpine, colchicine, and rubidium salts were found to affect specific behaviors of the fruit fly. The results allow some inferences about the chemical basis of Drosophila behavior and support the proposal to employ this organism in research on new drugs affecting behavior. 24 references. (Author abstract)

004433 Leyland, C. M.; Gwyther, R. J.; Rylands, J. M. Gwyther: Chemical Defense Establishment, Porton Down, Salisbury, Wiltshire, England **An improved method for detecting drug effects in the open field.** Psychopharmacology. 63(1):33-37, 1979.

A double test crossover design was applied to the testing of rats in the open field. When used to examine the effects of atropine, chlorpromazine, and lysergic acid diethylamide (LSD) on open field behavior, this design proved from 4 to 40 times more sensitive than the previously popular single test design. In no case was the double test design less sensitive. Results are discussed in relation to screening of medically useful compounds. 23 references. (Author abstract)

004434 Mann, Stephen P. ARC Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **Assay of tyrosine hydroxylase in tissue homogenates: effects of Triton-X, sodium, calcium and cyclic AMP.** Biochemical Pharmacology. 29(11):1593-1595, 1980.

The effects of NaC1, CaC12, Triton X-100, and cyclic AMP on homogenates of guinea-pig caudate nucleus were examined and a new assay for tyrosine hydroxylase (TH) in homogenates and small pieces of tissue is described. It appears that freely accessible TH can be activated by cations and that Triton X-100 and the acetone powder procedure are both good methods of making the enzyme easily accessible to substrates. Values obtained using Triton X-100 and activating ions on whole homogenates have again shown that the amounts of TH in the caudate nucleus are greater than earlier observations, indicating that the caudate nucleus has a considerable capability for the synthesis of L-dopa under optimal conditions. It is concluded that the Triton X-100/Nac1 incubation mixture is suitable for the assay of TH in all cases where the measurement of maximal activity is required. 9 references.

004435 Mumford, L.; Teixeira, A. R.; Kumar, R. Kumar: Institute of Psychiatry, De Crespigny Park, London SE5 8AF, England **Sources of variation in locomotor activity and stereotypy in rats treated with d-amphetamine.** Psychopharmacology. 62(3):241-245, 1979.

The effects of changes in procedural variables in tests of motor activity were examind using rats treated with amphetamine. Treated rats were observed continuously in either an enclosed Y-maze or on an elevated Y-shaped platform. Patterns of increased walking and sterotypy were unaffected by the type of apparatus but rearing remained totally suppressed at all dose levels on the elevated platforms. In a second experiment, groups of rats were given single short tests in the enclosed Y-maze, which was novel to them. The stimulant actions of amphetamine on locomotion were obscured by high baseline levels of motor activity induced by the novel environment. It is concluded that continuous measurements of habituated rats may provide a more sensitive means of evaluating stimulant actions of drugs in screening tests. 17 references. (Author abstract modified)

004436 Naggar, Viviane F.; Daabis, N. A. Dept. of Pharmaceutics, Faculty of Pharmacy, University of Alexandria, Alexandria, Egypt **An in vitro study of the interaction between diazepam and casein.** Scientia Pharmaceutica. 48(2):101-110, 1980.

The effect of casein on the dissolution behavior of diazepam from suspension in hydrochloric acid was investigated using a dissolution dialysis technique. Casein reduced the dialysis rate of the tranquilizer obviously. Adsorption studies were performed and diazepam was found to adsorbed on casein and its elution was relatively low. The effect of some drugs on additives on adsorption was also tested. The highest suppressive effect was shown by citric acid. Surfactants had an intermediate suppressive effect, urea had a slight effect while glycine, phenazone, ethosuximide, metformin hydrochloride and polyethylene glycol 600 had a negligible effect. Sodium benzoate, dibasic calcium phosphate, and monobasic sodium phosphate gave an adverse action. 20 references. (Author abstract modified)

004437 Overo, K. Fredricson Biochemical Dept. H. Lundbeck and Company A/S, Ottiliavej 7-9, DK-2500 Copenhagen/ Valby, Denmark **A specific fluorimetric method for assay of drug levels in serum of patients treated with clopenthixol decanoate injections.** Acta Psychiatrica Scandinavica. 61(Supplementum 279):92-103, 1980.

A fluorimetric method is presented for the simultaneous and specific assay in serum of clopenthixol decanoate, clopenthixol and a clopenthixol metabolite, deprived of the ethanol group in the side chain. The separation is achieved by extractions and thin layer chromatography and fluorescence brought about by treatment with sulphuric acid. The limit of detection in 3 ml serum samples is about 2 ng/ml for clopenthixol and metabolite, and somewhat higher for the ester. In addition, serum data are presented for schizophrenic patients treated with intramuscular

injection of 100 to 600mg clopenthixol decanoate in Visoleo every second week. Relatively stable (mean maximum/minimum ratio about 2; maximum after 3 to 7 days) clopenthixol levels were recorded throughout the dosage interval. Somewhat lower metabolite levels were found. There was no evidence for the presence of clopenthixol decanoate. 7 references. (Author abstract)

004438 Poling, Alan; Cleary, James; Monaghan, Michael. Dept. of Psychology, Western Michigan University, Kalamazoo, MI 49008 **The use of human observers in psychopharmacological research.** Pharmacology Biochemistry and Behavior. 13(2):243-246, 1980.

The use of human observers in nonhuman drug studies is discussed. A review of the literature from 1974 to 1978 indicates that many studies fail to use interobserver agreement. Procedures designed to enhance the credibility of data are more often followed in applied behavioral analysis and related behavioral sciences than in psychopharmacology. 27 references. (Author abstract modified)

004439 Pollard, G. T.; Howard, J. L. Dept. of Pharmacology, Wellcome Research Laboratories, 3030 Cornwallis Rd., Research Triangle Park, NC 27709 **The Geller-Seifter conflict paradigm with incremental shock.** Psychopharmacology. 62(2):117-121, 1979.

A study to determine whether an incremental shock conflict paradigm serves the drug specificity requirements of the original Geller-Seifter paradigm is reported. The typical Geller-Seifter conflict paradigm for predicting clinical efficacy of anxiolytics is a multiple variable-interval/continuous reinforcement availability (CRF) schedule in which response rates in the CRF (conflict) portion are depressed by response contingent electric shock. In 1 hour sessions, anxiolytics raise the depressed conflict rate. Recently, it was shown that replacing the single shock level with an arrangement whereby shock begins at zero and is increased with each response in the conflict portion produced more orderly data and facilitated training and maintenance of experimental subjects; chlordiazepoxide was the test drug. Those results are replicated in 30 minute sessions and the incremental paradigm is demonstrated to be as specific for anxiolytics as the standard Geller-Seifter paradigm. The possibliity of very short sessions is suggested. 22 references. (Author abstract modified)

004440 Puglisi-Allegra, Stefano; Renzi, Paolo. Istituto di Psicobiologia e Psicofarmacologia, CNR via Reno, 1-00198 Rome, Italy **An automated device for screening the effects of psychotropic drugs on aggression and motor activity in mice.** Pharmacology Biochemistry and Behavior. 13(2):287-290, 1980.

An automated technique for measuring aggressive behavior and motor activity in mice is described. The method permits both behaviors to be measured continously for long periods of time without disturbing the animals except for feeding, watering, and cage cleaning. This method was used to study the effects of n-D-propylacetate, which alters fighting behaviors without affecting motor activity. 9 references. (Author abstract modified)

004441 Reinhard, John F., Jr.; Moskowitz, Michael A.; Sved, Alan F.; Fernstrom, John D. Laboratory of Neural and Endocrine Regulation, Massachusetts Institute of Technology, Cambridge, MA 02139 **A simple, sensitive and reliable assay for serotonin and 5-HIAA in brain tissue using liquid chromatography with electrochemical detection.** Life Sciences. 27(11):905-911, 1980.

A simple, sensitive method for simultaneous measurement of serotonin and 5-hydroxyindoleacetic acid is described. As little as 22 picograms of serotonin and its deaminated metabolite can be detected in deproteinated brain samples with this method, which uses liquid chromatography and electrochemical detection. 20 references. (Author abstract modified)

004442 Vanuytven, M.; Vermeire, J.; Niemegeers, C. J. E. Niemegeers: Dept. of Pharmacology, Janssen Pharmaceutical Research Laboratories, B-2340 Beerse, Belgium **A new motility meter based on the Doppler principle.** Psychopharmacology. 64(3):333-336, 1979.

A new motility meter for recording the locomotor activity of small laboratory ani mals is presented, and its use in a study of the locomotor effects of d,l-amphetamine and haloperidol is described. The equipment is designed to record simultaneously, but independently, the motility of eight animals (or groups of animals) in separate cages. The functional mechanism is an application of the Doppler principle. The use of electromagnetic waves presents the important advantages of contactless detection and freedom from interference of external stimuli with spontaneous activity. Both horizontal and vertical components of movement are registered. Motility, as measured with the Doppler motility meter, proved to be very sensitive to drug effects. 11 references. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

004443 Hindmarch, I.; Parrott, A. C. Dept. of Psychology, University of Leeds, Leeds LS2 9JT, England **The effects of combined sedative and anxiolytic preparations on subjective aspects of sleep and objective measures of arousal and performance the morning following nocturnal medication: I. acute doses.** Arzneimittel Forschung. 30(6):1025-1028, 1980.

The effects of acute doses of various sedative and anxiolytic preparations on subjective and objective assessments of sleep and early morning behavior were studied with human volunteers. Nitrazepam was used as the benzodiazepine hypnotic, dichloralphenazone as the standard nonbenzodiazepine hypnotic, and clobazam as the representative anxiolytic preparation. The acute dose nature of the experimental design produced variable results, but a degree of disruption of performance the morning following nocturnal medication was measured. This finding suggested that anxiolytics and sedatives might potentiate one another and the resulting disorganization of behavior might be important in patient populations having to drive motor vehicles. 18 references. (Author abstract modified)

004444 Meltzer, Herbert Y.; Fang, Victor S.; Young, Michael A. Dept. of Psychiatry, University of Chicago, Pritzker School of Medicine, Chicago, IL **Clozapine-like drugs.** Psychopharmacology Bulletin. 16(3):32-35, 1980

Drugs which share some, but not all of the characteristics of clozapine (a dibenzodiazepine antipsychotic drug in widespread clinical use in Europe, but withdrawn from clinical testing in the US because of an apparently higher incidence of agranulocytosis than other antipsychotic drugs), are described. It is noted that the great interest in clozapine is based on its very low incidence of extrapyramidal side-effects (EPS) and the possibility that it might not produce tardive dyskinesia following chronic usage. It is suggested that clozapine-like drugs may be found in all the major classes of antipsychotic agents. The key issue is the nature of the screening used to identify the drugs. No one test appears sufficient. Conceivably, low EPS in man plus reduced effect on prolactin secretion may be a sufficient means of identifying clozapine-like drugs. 13 references.

004445 Rudenko, G. M.; Altshuler, R. A. Pharmacological Committee, Rossolimo Str. 11, Moscow 09-435, USSR **Peculiarities of clinical activity and pharmacokinetics of sydnocarb (sydnocarbum), an original psychostimulant.** Aggressologie. 20(D):265-270, 1979.

The results of clinical trials of sydnocarb, a new psychostimulant developed in the USSR, on 493 patients are reported. In the overwhelming majority of cases, sydnocarb produced a marked psychostimulating effect, raising the tempo of mental and physical activity, increasing locomotor and speech activity, and producing sthenic symptoms within 30 to 60 minutes after the first dose, with effects persisting for 6 to 8 hours. Sydnocarb was most effective in patients whose state was characterized by asthenic and hypoergic symptoms, with good results in 93.7% of these cases. Sydnocarb also proved effective with healthy subjects in cases of weariness as a result of mental strain of physical overwork. No success was achieved in cases of depressions with complex structure of more severe psychopathological state. Comparative pharmacological investigations of sydnocarb in the mouse are also discussed. 13 references.

004446 Sitaram, N.; Moore, Angela M.; Gillin, J. Christian. National Institute of Mental Health, Building 10, Room 3N224, Bethesda, MD 20205 **Scopolamine-induced muscarinic supersensitivity in normal man: changes in sleep.** Psychiatry Research. 1(1):9-16, 1979.

The effect of scopolamine on human subjects during sleep was studied. Scopolamine (6mcg/kg) was administered on 3 consecutive mornings to normal human subjects. Sleep recordings obtained at night (when the central anticholinergic effect of the morning scopolamine was no longer present) indicated a significant reduction in latency to REM sleep onset on the nights following the second and third injections. This effect is opposite to the direct pharmacological action of nighttime administration of scopolamine (i.e., prolongation of REM latency). In addition, total sleep time and sleep efficiency were reduced, and sleep latency was increased. Scopolamine pretreatment on 2 consecutive mornings also potentiated the REM inducing effect of arecoline, a central muscarinic agonist. These data are consistent with the development of cholinergic supersensitivity following cholinergic blockage. 16 references. (Author abstract modified)

004447 Tallone, G.; Ghirardi, P.; Bianchi, M. Cesa; Ravaccia, F.; Bruni, G.; Loreti, P. Ghirardi: Sezione Ricerche Mediche, Simes S.p.A, Via Bellerio 41, I-20161 Milano, Italy **Reaction time to acoustic or visual stimuli after administration of camazepam and diazepam in man.** Arzneimittel Forschung. 30(6):1021-1024, 1980.

The comparative effects of visual and acoustic-induced reactions times of Camazepam, a new anxiolytic benzodiazepine with weak muscle relaxant and hypnotic effects, diazepam, and a placebo were studied. Using a double-blind crossover design with 11 healthy human Ss, the response to acoustic stimula was more rapid than that to visual stimuli with all three treatments. The pattern of reaction times after camazepam was similar to that after placebo; diazepam retarded reaction times, with the maximum effect 1 hour after administration. Reaction times were not altered by a single dose of camazepam, but they were lengthened by a single dose of diazepam, in comparison with the placebo. An anxiolytic effect without alteration of physical performance resulted from 10mg of camazepam. 20 references. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

004448 Ahlfors, U. G.; Dencker, S. J.; Gravem, A.; Renvig, J. Hesperia Hospital, SF-00260 Helsingfors 26, Finland **Clopenthixol decanoate and perphenazine enanthate in schizophrenic patients: a double-blind Nordic multicentre trial.** Acta Psychiatrica Scandinavica. 61(Supplementum 279):77-91, 1980.

Clinical properties of clopenthixol decanoate and perphenazine enanthate were compared in a double-blind multicenter trial involving 172 schizophrenic inpatients at 14 psychiatric hospitals in Finland, Sweden, and Norway. Although test treatment was initiated in 172 chronic schizophrenics, the planned 6 month test period was completed by 57 patients receiving depot clopenthixol and 48 receiving depot perphenazine. The therapeutic effect was assessed by means of the Clinical Global Impressions, the Brief Psychiatric Rating Scale (BPRS), and the Nurses' Observaton Scale for In-Patient Evaluation (NOSIE 30) and was found significant for both test drugs. Significant differences in the effect were seen only in hostile suspiciousness (BPRS) and social interest (NOSIE 30). For these items, clopenthixol decanoate was found superior to perphenazine enanthate. The influence of side-effects on the patients' functioning was found to be slightly, but nonsignificantly, more troublesome for the perphen-

azine ananthate patients. 11 references. (Author abstract modified)

004449 Aref, Mohamed A.; El-Guindy, Trandil A. Mental Hospital, Kuwait **Pipothiazine palmitate in the long-term treatment of schizophrenia.** Journal of International Medical Research. 8(4):293-294, 1980.

Fifty patients suffering from active schizophrenic episodes were treated with electroplexy and thioproperazine for 3 weeks. Pipothiazine palmitate was then given parenterally at a dose of 100 mg at 4 week intervals over a period of 3 years. It seemed to be effective in maintaining remissions in 48 patients.

004450 Bertoletti, P.; Fusco, A.; Calvani, M.; Nava, D. Ospedale Psichiatrico Santa Maria della Pieta, Rome, Italy **/5-HTP in therapy of depression and schizophrenia (a clinical and psychological experimental study of 26 consecutive cases)./** Il 5-HTP nella terapia della depressione e della schizofrenia (studio sperimentale clinico e psicologico su 26 casi consecutivi). Rivista di Neuropsichiatria e Scienze Affini. 25(2):69-88, 1979.

The utilization of 5-HTP in the therapy of depression and schizophrenia was studied in 26 psychiatric patients. Ten were affected with depressive syndrome, five with hebephrenic schizophrenia, seven with paranoid schizophrenia, and four with schizophrenic excitability. The depressed subjects were administered 100mg of 5-HTP three times daily for a duration of 30 days. The schizophrenic subjects received six capsules daily for a total of 20 days. Results, clinically evaluated with the Hamilton and Witterborn tests, indicate the efficacy of the drug for depression and hebephrenic schizophrenia, but not in schizophrenic excitability. It is concluded that the results favor the aminic hypothesis of psychic illness and reproposes the hypothesis that schizophrenic illness does not exist, but schizophrenia does. 51 references. (Author abstract modified)

004451 Branchey, Marc H.; Brebbia, D. Robert; Cooper, Thomas B.; Simpson, George M. Rockland Research Institute, Orangeburg, NY 10962 **Effects of loxapine on the sleep of chronic schizophrenics.** Psychopharmacology. 62(2):201-206, 1979.

The sleep patterns of four male chronic schizophrenic patients were monitored throughout the various phases of a 1 year therapeutic trial with loxapine succinate, a newly developed neuroleptic. Compared with the initial drug free baseline, the early drug period was characterized by an increase in REM percentage, REM density, and REM activity. During the drug maintenance period, the increase in REM phasic events was accompanied by an increase in total sleep. Severe insomnia was noted during the initial period of drug withdrawal. The absence of time lag between changes in drug administration schedule and the associated alterations in sleep patterns was in contrast with the time latency of the therapeutic response. This is probably an indication that the effects of this neuroleptic on sleep and on psychopathology are mediated by different mechanisms. 18 references. (Author abstract)

004452 Brenner, Ronald; Shopsin, Baron. Bronx State Hospital, Albert Einstein School of Medicine, Bronx, NY 10461 **The use of monoamine oxidase inhibitors in schizophrenia.** Biological Psychiatry. 15(4):633-647, 1980.

A literature review was undertaken to assess the potential therapeutic effects of monoamine oxidase (MAO) inhibitors in schizophrenic individuals. The review covered the global outcome in 281 patients gathered from 14 studies. The results of double-blind studies, support open trials, and other anecdotal data indicate that MAO inhibitor therapy in chronically ill schizophrenic populations has met with a very small and statistically insignificant incidence of symptom illness aggravation. The data indicate that of 281 patients given an MAO inhibitor, 71% showed no change, 3% worsened and 26% showed symptom improvement. Types of MAO inhibitor, dosage and treatment duration, and side-effects are discussed. 51 references.

004453 Dencker, S. J.; Frankenberg, K.; Hansen, V.; Malm, U. Dept. II, Lillhagen Hospital, Box 3005, S-422 03 Hisings Backa 3, Sweden **Clopenthixol and flupenthixol depot preparations in outpatient schizophrenics: II. Factor analysis of the CPRS subscale for schizophrenia.** Acta Psychiatrica Scandinavica. 61(Supplementum 279):29-40, 1980.

Comprehensive Psychopathological Rating Scale (CPRS) results from a longitudinal study of depot clopenthixol and flupenthixol in maintenance treatment of 60 schizophrenic outpatients were subjected to factor analysis. Eleven factors were identified: anxiety/depression/asthenia; observed emotions; psychotic; motor; other hallucinations; affect fluctuation; sensory disturbance; side-effects; organic; incongruous emotional displays; and sleep. These 11 CPRS factors can be used for monitoring the treatment process as to doses of psychopharmaceutical drugs as well as indications for other methods of treatment, e.g. psychosocial therapy programs. CPRS results are compared with those for two other clinical ratings scales. 7 references. (Author abstract modified)

004454 Dencker, S. J.; Lepp, M.; Malm, U. Dept. II, Lillhagen Hospital, Box 3005, S-422 03 Hisings Backa 3, Sweden **Clopenthixol and flupenthixol depot preparations in outpatient schizophrenics. I. A one year double-blind study of clopenthixol decanoate and flupenthixol palmitate.** Acta Psychiatrica Scandinavica. 61(Supplementum 279):10-28, 1980.

In a 1 year double-blind study, clopenthixol decanoate and flupenthixol palmitate, both depot neuroleptics of the thioxanthene group, were examined in 60 deinstitutionalized chronic schizophrenics, using 4 week intervals between injections. A major aim was to study the two drugs under maintenance treatment conditions in an outpatient setting. All subjects had undergone earlier hospital admission and rehabilitation training periods, had been treated with depot neuroleptics in the last 3 years, and had been free of relapse for at least 15 months. Ten patients dropped out, seven because of unsatisfactory effect, primarily as a result of design limitations on acceptable dose levels. Despite earlier long-lasting neuroleptic treatment and the good social adaptation in this schizophrenic subgroup, there was an observed symptom decrease in all the rating scales. Both drugs appeared particularly effective in reducing psychopathology related to withdrawal, retardation, anxiety/depression/asthenia factors and observed emotions and affect fluctuations. Side-effects were slight for both drugs at 12 months. The improvement in psychopathology, although not in community functioning (social and work), with optimal results after 6 months, appeared to be a combined result of drug efficiency and careful monitoring of drug levels. 26 references. (Author abstract modified)

004455 Dencker, S. J.; Lepp, M.; Malm, U. Dept. II, Lillhagen Hospital, Box 3005, S-422 03 Hisings Backa 3, Sweden **Do schizophrenics well adapted in the community need neuroleptics? A depot neuroleptic withdrawal study.** Acta Psychiatrica Scandinavica. 61(Supplementum 279):64-76, 1980.

Two depot neuroleptics (flupenthixol palmitate and clopenthixol decanoate) used for at least 15 months were withdrawn in 32 schizophrenic outpatients belonging to the most symptom free and social cohort of a total patient population. They all had only slight schizophrenic symptoms, were well adapted in the community, and had been free from relapse for at least 2 years before the study. They were assessed by means of rating scales every month during the first 6 months and then after 9 and 12

months. After the 1 year trial, 26 patients had relapsed. Moreover, an additional four of the six nonrelapsing patients relapsed during the second drug free year. The results indicate the necessity of along followup period after withdrawal of depot neuroleptics. Moreover, the results suggest that periodical drug free periods of about 3 months are appropriate in symptom poor patients during long-term treatment with long-acting antipsychotic drugs. 18 references. (Author abstract)

004456 Dencker, S. J.; Malm, U.; Jorgensen, A.; Overo, K. Fredricson. Dept. II, Lillhagen Hospital, Box 3005, S-422 03 Hisings Backa 3, Sweden **Clopenthixol and flupenthixol depot preparations in outpatient schizophrenics. IV. Serum levels and clinical outcome.** Acta Psychiatrica Scandinavica. 61(Supplementum 279):55-63, 1980.

Two pharmacokinetic parameters, minimum serum concentration in the dosage level and area under the serum concentration curve, were correlated to 14 parameters for clinical outcome (total points and factor points from the Brief Psychiatric Rating Scale, the Comprehensive Psychopathological Rating Scale, and a side-effects scale) in a double-blind clinical trial of clopenthixol and flupenthixol depot preparations in outpatient schizophrenics. No statistically significant correlations were observed. It is of some interest, however, that results suggested that the treatment of individual patients with neuroleptics may be adjusted by means of repeated ratings, residual percentage, changes in psychopathology, and determinations of serum concentrations. Results do not indicate any optimal concentration range for these depot neuroleptics in the maintenance phase of schizophrenia. The so called therapeutic window obviously varies with the phase of the disease as well as the patient's social situation. 14 references. (Author abstract)

004457 Diamond, Stuart J.; Scammell, Robert E.; Pryce, Ivor G.; Huws, Dafydd; Gray, Charles. Dept. of Psychology, University College, Cardiff, Wales **Some effects of piracetam (UCB 6215 Nootropyl) on chronic schizophrenia.** Psychopharmacology. 64(3):341-348, 1979.

The effects of a nootropic drug, piracetam (UCB 6215 Nootropyl) on chronic schizophrenia were investigated in 27 patients. Chronic schizophrenic patients showed improvement in object naming and in tests where the patient was required to indicate the number of times he had been trapped. Improvements were also noted in learning and memory tasks. In dichotic listening, the patients showed a reduction in the amount of incorrect verbal responses produced. There were no improvements in symptom rating or social behavior rating. These results suggest some cognitive improvement but little if any change in the disease state of the patient. 24 references. (Author abstract modified)

004458 Hamilton, M.; Card, I. R.; Wallis, G. G.; Mahmoud, M. R. Card: Dept. of Psychiatry, Leeds University, Leeds, England **A comparative trial of decanoates of flupenthixol and fluphenazine.** Psychopharmacology. 64(2):225-229, 1979.

A double-blind trial was carried out comparing the effects of decanoates of flupenthixol and fluphenazine on the symptoms, ward behavior, and functional capacity in occupational therapy of 51 chronic schizophrenic inpatients. Patients were carefully selected on the basis of rigid criteria for diagnosis. To exclude nonresponders to neuroleptics, the patients were first taken off neuroleptic drugs and only those who appeared to show deterioration were included in the trial. The dosage of drugs was varied according to clinical indications. The length of the trial was initially 4 months, and 31 patients were followed for an additional 4 months. To ensure reliability, multiple assessments were made at the start and at the end of the trial. Most of the statistical tests showed no differences between treatments, but some of those relating to affective symptoms showed an advantage for flupenthixol compared to fluphenazine. There were no differences in the incidence of extrapyramidal side-effects, which required treatment in only 32% of the patients on each drug. 21 references. (Author abstract)

004459 Hansell, Norris. Northwestern Institute of Psychiatry, 320 E. Huron Street, Chicago, IL 60611 **Approaching long-term neuroleptic treatment of schizophrenia.** Journal of the American Medical Association. 242(12):1293-1294, 1979.

Approaches to long-term neuroleptic treatment of schizophrenia are examined, and the fact that neuroleptic therapy can prevent acute episodes and may improve the level of function in chronic cases is emphasized. The hazards of tardive dyskinesia, however, require a rigorous design for any long-term program. The protocol includes narrow indications, demonstrations of efficacy and necessity, and arrangements for surveillance, cooperation, and emergency. Patient instruction improves the precision of medication use and may increase adaptive efforts during episodes. 8 references. (Author abstract modified)

004460 Hartmann, W.; Kind, J.; Meyer, J. E.; Muller, P.; Steuber, H. Meyer: Klinik fur Psychiatrie, Universitat Gottingen, von-Siebold-Strasse 5, D-3400 Gottingen, Germany **Neuroleptic drugs and the prevention of relapse in schizophrenia: a workshop report.** Schizophrenia Bulletin. 6(3):536-543, 1980.

Questions relating to neuroleptic drugs and the prevention of relapse in schizophrenics, addressed at a 3 day workshop sponsored by the German Research Foundation, are reported. Whether long-term psychopharmacotherapy can prevent relapse was examined. Another focus of discussion throughout the meeting was the problem of side-effects and toxicities associated with long-term neuroleptic treatment. Participants exchanged views on how to deal with these side-effects and how to treat relapses in patients withdrawn from medication. At the workshop's conclusion, participants attempted to summarize presently accepted treatment guidelines and considered unresolved questions such as the optimal dosage for prophylactic treatment and the criteria for determining which schizophrenic patients do or do not require maintenance medication. The workshop program, together with a list of participants and their addresses, is included. (Author abstract modified)

004461 Itoh, Hitoshi; Yagi, Gohei; Ohtsuka, Nobuo; Iwamura, Kenichiro; Ichikawa, Kazuo. Dept. of Neuropsychiatry, School of Medicine, Keio University, 35 Shinanomachi, Shinjukuku, Tokyo 160, Japan **Serum level of haloperidol and its clinical significance.** Progress in Neuro-Psychopharmacology. 4(2):171-183, 1980.

Blood concentrations of haloperidol were determined in schizophrenic patients by a recently developed radioimmunoassay following a single oral dose, in patients on long-term maintenance therapy, and following repeated doses of haloperidol. A significant positive correlation between blood concentration and the daily dose per kg of bodyweight was found, and a relationship between blood concentration and development of extrapyramidal symptoms was noted. The combined use of antiparkinsonian drugs failed to depress the blood level of haloperidol. The blood concentration of haloperidol varied more widely and required much more time in attaining a steady state after administration in a single dose than after administration in divided doses. 12 references. (Author abstract modified)

004462 Jorgensen, A.; Overo, K. Fredricson. H. Lundbeck and Company A/S, Ottiliavej 7-9, DK-2500 Valby, Copenhagen, Denmark **Clopenthixol and flupenthixol depot preparations in out-**

patient schizophrenics. III. Serum levels. Acta Psychiatrica Scandinavica. 61(Supplementum 279):41-54, 1980.

Serum concentrations during 4 week dosage intervals were determined for 45 schizophrenic outpatients receiving depot drug maintenance treatments of clopenthixol decanoate or flupenthixol palmitate (intramuscular injection). Maximal drug levels were attained by the end of the first week after injection of either preparation. A period of exponential decline was then recorded. Half-lives were estimated to 19 days for clopenthixol and 17 days for flupenthixol. These half-lives most likely refer to the rate of release from the oil depot, and not to elimination of the drug. The mean ratio between maximal and minimal drug levels was 2.5 for clopenthixol and 3.7 for flupenthixol. Systemic clearance was estimated to about .71/min and .51/min. Significant correlation was found between administered doses and recorded serum levels, between doses and estimated areas under the more limited individual variability than seen with other orally administered psychotropic drugs. Results clearly demonstrate that significant serum levels of active drug are maintained throughout the 4 week intramuscular dosage interval. 28 references. (Author abstract modified)

004463 Lindstrom, Leif H.; Persson, Eva. Psychiatric Research Center, Ulleraker Hospital, S-750 17 Uppsala, Sweden **Propranolol in chronic schizophrenia: a controlled study in neuroleptic-treated patients.** British Journal of Psychiatry. 137(August):126-130, 1980.

The effect of the beta-blocker propranolol at a dose level of 1280 to 1920mg per day was studied with a double-blind cross-over design in 12 chronic schizophrenics. All Ss had shown persistent psychotic symptoms despite maintenance treatment with a depot neuroleptic. By use of a psychiatric rating scale, an improvement was seen during the 2 week treatment period in six patients, whereas three patients were unchanged and three deteriorated. The effect on total symptom scores for the whole group was significantly better after propranolol than before. The data indicate that propranolol in high doses has an antipsychotic effect in some schizophrenic patients who are receiving neuroleptics. 16 references. (Author abstract)

004464 Lykouras, E.; Varsou, E.; Rinieris, P.; Stefanis, C. N. Stefanis: Dept. of Psychiatry, Eginition Hospital, 74 Vas. Sophias Avenue, Athens University, Athens, Greece **Plasma cyclic AMP in schizophrenics.** Progress in Neuro-Psychopharmacology. 4(1):69-74, 1980.

Concentrations of cyclic AMP were studied by a protein binding assay in the plasma of 39 inpatients with various types of schizophrenic disorders. There was no difference in cyclic AMP levels between patients and controls. No difference was noted when schizophrenic diagnostic subgroups and control Ss were compared. Eleven schizophrenic Ss who were given chlorpromazine (300mg daily for one month) showed a significant decrease of plasma cyclic AMP which paralleled the clilnical improvement. Results are discussed in relation to the dopaminergic hypothesis of schizophrenia and the effect of neuroleptic drugs on cyclic AMP metabolism. 16 references. (Author abstract modified)

004465 Modai, Ilan; Rotman, Avner; Munitz, Hanan; Tjano, Shumel; Wijsenbeek, Henricus. Rotman: Dept. of Membrane Research, Weizmann Institute of Science, Rehovot, Israel **Serotonin uptake by blood platelets of acute schizophrenic patients.** Psychopharmacology. 64(2):193-195, 1979.

Active uptake of serotonin by blook platelets was compared for ten acute schizophrenic inpatients and ten health controls. The patients were under treatment with clhorpromazine (n=7), diazepam, pericyazine, or thioridazine (1 patient each). Preliminary results of biochemical assays indicated that serotonin uptake in the schizophrenic group was about 40% lower than that in controls. Patients were followed over a period of 5 weeks with no significant change in uptake. The lack of change in the rate of uptake with time might be indicative of genetic defect in the presynaptic plasma membrane rather than a reversible defect parallel to the schizophrenic syndrome. Directions for further research are briefly noted. 13 references. (Author abstract modified)

004466 Nahunek, K.; Svestka, J.; Ceskova, E. Psychiatric Clinic Medical Faculty, J. E. Purkyne University, Brno, Czechoslovakia **Further clinical experiences with optical isomers of the L and D clorothepin.** Agressologie. 20(D):275-278, 1979.

The therapeutic efficacy of D-clorothepin, L-clorothepin, and clorothepin racemate was tested on 47 hospitalized schizophrenics. In the first 3 weeks, two thirds and more of the total psychopathology was reduced by the tested drugs, the greatest reduction occurring during the first week. After 6 weeks, racemate of clorothepin showed the greatest reduction in total pathology, 61%, while L-clorothepin showed the least, 34%. As to side-effects, a higher frequence of extrapyramidal symptoms and akathisia plus dyskinesia were found with the D-form and the racemate than with the L-form. In a comparison of the therapeutic efficacy after 3 and 6 weeks, the same results were achieved in 43%, an apparent retreat trend was seen in 53%, and only in 4% were the results different. 4 references.

004467 Nedopil, N.; Ruther, E. Ruther: Psychiatrische Klinik der Universitat, Nussbaumstr. 7, D-8000 Munich 2, Germany **Effects of the synthetic analogue of methionine enkephalin FK 33-824 on psychotic symptoms.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(3):277-280, 1979.

To determine the antipsychotic efficacy of FK 33-824 in schizophrenics, nine schizophrenic patients were treated with FK 33-824 on two consecutive days in a dose of 0.5mg on the first day, and 1.0mg on the second. Three patients refused therapy during or after the first infusion. Results show that of the remaining six patients (two hebephrenic, four paranoid), five patients improved significantly on the first and second day. The total Brief Psychiatric Rating Scale (BPRS) and four of the five BPRS factors were reduced significantly the day after treatment relative to pretreatment values. The improvement continued for 28 to 168 hours. Results are consistent with other reports suggesting the therapeutic value of beta-endorphins in psychotic patients. 14 references. (Author abstract modified)

004468 Rigler, Tonka; Sisek, Ivo. Psihijatrijska bolnica Jankomir, Zagreb, Yugoslavia **/Ten years' experience with the treatment of schizophrenics using fluphenazine decanoate./** Nase desetogodisnje iskustvo u lijecenju shizofrenih bolesnika flufenazin-dekanotom. Socijalna Psihijatrija. 7(2):177-181, 1979.

A group of 53 male and female schizophrenics who were treated with fluphenazine decanoate were followed up for a period of 10 years (1969-1979). Psychological status and social adjustment were observed. The side-effects of long-term medication were followed up with laboratory controls. Results show that 24 patients (43.3%) remained in social psychological remission. The other 29 Ss showed relapses which required hospitalization. The findings are in agreement with those of other studies emphasizing the need for continuous medication in schizophrenic psychosis, to enable patients to function fully in the working world and in social situations. Sociotherapy is recommended as an accompanying measure in the treatment of schizophrenic psychosis. 11 references. (Journal abstract modified)

004469 Sakurai, Yukihiko; Takahashi, Ryo; Nakahara, Tadahiko; Ikenaga, Hiroshi. Takahashi: Dept. of Neuropsychiatry,

Nagasaki University School of Medicine, 7-1 Sakamoto-machi, Nagasaki 853, Japan **Prediction of response to and actual outcome of chlorpromazine treatment in schizophrenic patients.** Archives of General Psychiatry. 37(9):1057-1062, 1980.

The prediction of response to chlorpromazine treatment in 37 schizophrenics was evaluated in a blind controlled study on the basis of actual outcomes. Prior to the initiation of treatment, blood samples were taken 3 hours after a dose of 50mg of chlorpromazine for the analyses of the drug and its metabolites. The chlorpromazine therapy was then begun and continued for 3 months. The results agree with previous conclusions that patients who show high levels of metabolites after a single dose of chlorpromazine tend to have poor clinical improvement with chlorpromazine and that the responders show the opposite pattern. The predictability of response to chlorpromazine therapy is significantly high in patients with very low or high levels of the metabolites; however, this is useful at best in 46% of the subjects studied. 28 references. (Author abstract)

004470 Smith, Robert C.; Tamminga, Carol A.; Crayton, John W.; Dekirmenjian, Haroutune; Davis, John M. Behavioral Neurochemistry Section, Texas Research Institute of Mental Science, 1300 Moursund, Texas Medical Center Houston, TX 77030 **Relationship of butaperazine blood levels to plasma prolactin in chronic schizophrenic patients.** Psychopharmacology. 66(1):29-33, 1979.

The relationship of plasma prolactin to plasma or red blood cell butaperazine levels was investigated in chronic schizophrenic patients treated with clinical doses of butaperazine, both after a single acute dose of the drug and during regular, twice daily butaperazine administration. Although there was a significant curvilinear relationship between peak plasma butaperazine levels after an acute single oral dose of butaperazine and the maximum prolactin response, steady state levels of plasma or red cell butaperazine and plasma prolactin were not related. It is concluded that plasma prolactin cannot be used as a substitute for, or even as a rough indicator of, butaperazine blood levels in chronic schizophrenic patients being treated with clinical doses of butaperazine. 19 references. (Author abstract)

004471 Versiani, Marcio. Av. N. S. Copacabana, 1133 conj. 1303, 22070 Rio de Janeiro, Brazil **/Therapeutics IV -- pharmacological treatment of schizophrenia./** Terapeutica IV -- o tratamento farmacologico da esquizofrenia. Jornal Brasileiro de Psiquiatria. 29(3):181-186, 1980.

Problems that occur during the pharmacological treatment of schizophrenia are examined. In different case studies of schizophrenics treated with antipsychotics, one patient demonstrated dyskinesia, one recovered completely, one reached a severe residual state to be maintained with a small dosage, and one needed a larger dosage due to the severity of the schizophrenia. Patients being administered antipsychotic drugs can be divided into three groups relative to the efficiency of the drug. Examples of antipsychotic drugs and the groups in which they are placed are described. 5 references. (Journal abstract modified)

004472 Waehrens, J.; Gerlach, J. Gerlach: Sct. Hans Hospital, Dept. H, DK-4000 Roskilde, Denmark **Antidepressant drugs in anergic schizophrenia: a double-blind cross-over study with maprotiline and placebo.** Acta Psychiatrica Scandinavica. 61(5):438-444, 1980.

The possible activating effect of maprotiline, a relatively specific noradrenaline-reuptake inhibitor, was investigated in a double-blind crossover study of 17 inactive and emotionally withdrawn schizophrenics under long-term neuroleptic treatment. No significant differences with respect to either the level of activity or schizophrenic symptoms were found between maprotiline (mean dose 138mg/day) and placebo. Maprotiline provoked a slight psychotic exacerbation in one patient and sedation in another, four patients developed orthostatic hypotension, and two had an epileptic seizure. In the light of this and other studies, it is concluded that antidepressant drugs do not represent any therapeutic advance in the treatment of inactive schizophrenic patients receiving neuroleptics. 24 references. (Author abstract)

004473 Wistedt, Borje; Andersson, Lisbeth. Psykiatriska kliniken, Centrallasarettet, S-721 89 Vasteras, Sweden **/How do psychiatric patients perceive depot treatment: as a help or as addictive?/ /**Hur upplever den psykiatriska patienten depabehandling? Tvang eller hjalp? Nordisk Psykiatrisk Tidsskrift. 33(2):94-101, 1979.

A survey was conducted with 73 Swedish patients undergoing injection treatment (depot with neuroleptics) to determine the respondent's perceptions of this treatment regime in the wake of the public controversy which suggests that the treatment is addictive. Of the subjects, 38 were treated with Siqualone decanoat, 26 with Frialafon enantat, and nine with Flupenxithol decanoat. The median age of the sample was 46.6. The majority of subjects had been diagnosed as schizophrenics, and patients, receiving injections were on a regular dose ranging from once a week to once every 6 weeks, had been under treatment from 1.5 months to 6 years. Analysis of survey results indicates that more than 60% of the patients were satisfied with the treatment and did not perceive it as addictive. The positive response was not related to any age or treatment group, although elderly patients were more likely to complain of side-effects. 7 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

004474 Ballenger, James C.; Post, Robert M. Post: NIH, 9000 Rockville Pike, Bldg 10, Rm. 3S239, Bethesda, MD 20205 **Carbamazepine in manic-depressive illness: a new treatment.** American Journal of Psychiatry. 137(7):782-790, 1980.

A double-blind, placebo controlled trial of carbamazepine (Tegretol), a drug of choice for treatment of temporal lobe epilepsy, in manic-depressive patients is described. Seven of nine manic patients had a partial to marked response; several also showed relapses when placebo was substituted and improvement when carbamazepine was reinstituted. Five of 13 depressed patients showed significant improvement in depression ratings; three additional patients experienced partial relapse when placebo was substituted. Carbamazepine might also have prophylactic as well as acute efficacy in patients with both phases of manic-depressive illness, including some patients who do not respond to lithium. Therapeutic effects were achieved with 600 to 1600mg/day at blood levels of 8 to 12micrograms/ml with relatively few side effects. It is concluded that carbamazepine may prove to be a useful additional treatment for affective illness. 80 references. (Author abstract modified)

004475 Casey, Daniel E. Dept. of Medical Research and Psychiatry, Portland VA Hospital, Portland, OR 97207 **Mood alterations during deanol therapy.** Psychopharmacology. 62(2):187-191, 1979.

The hypothesis that an imbalance between central cholinergic and adrenergic influences may affect mood disorders was tested with 38 patients taking high doses of deanol, a putative acetylcholine precursor. Eight of the patients developed changes in mood: five became depressed and three became hypomanic. A predisposition is suggested as seven of these eight patients had histories of affective symptoms. There was no relationship between the changes in dyskinesias and mood. Theses observations have both practical and heuristic implications for the manage-

ment of patients and for further research into the pharmacology of affective disorders and deanol. 40 references. (Author abstract modified)

004476 Choi, Sin J.; Derman, Robert M. Psychiatry Service, Veterans Administration Medical Center, Northport, Long Island, NY 11768 **Lithium and cholinesterase.** Progress in Neuro-Psychopharmacology. 4(1):107-109, 1980.

The effects of lithium or serum cholinesterase in four patients suffering from endogenous depression were investigated in an attempt to elucidate the antimanic and antidepressant effects of lithium. Lithium was found to reversibly inhibit serum cholinesterase activity. Serum cholinesterase levels 2 hours after lithium treatment were significantly lower than those before treatment with lithium. However, serum cholinesterase levels 12 hours after lithium treatment were increased to levels which were not significantly different from those of the pretreatment of lithium levels. It is suggested that lithium may interact with cholinergic as well as adrenergic mechanisms to exert its antimanic and antidepressant effects. 6 references. (Author abstract modified)

004477 Cookson, J. C.; Silverstone, T.; Wells, B. Medical College of St. Bartholomew's Hospital, German Hospital, Ritson Road, London E8 1DF, England **A double-blind controlled study of pimozide vs chlorpromazine in mania.** Neuropharmacology. 18(12):1011-1013, 1979.

The antimanic effects of pimozide (PMZ), a neuroleptic of the diphenylbutylpiperidine series with specific dopamine receptor blocking activity, were compared with those of chlorpromazine (CPZ) in a double-blind trial. Manic in patients were given the maximum tolerated drug dose, up to 1600mg CPZ or 32mg PMZ daily in divided doses for up to 14 days. Improvements in clinical ratings were observed with either drug. Scores on the mania rating scale showed greater improvement with CPZ than with PMZ in the first 3 days, but PMZ was more effective on days 7 to 14. Sedation was noted in only 2 patients, all on PMZ. Results indicate that the core symptoms of manias can be improved by PMZ in some patients in the absence of sedation. 10 references.

004478 Cookson, J. C.; Silverstone, T.; Wells, B. Medical College of St. Bartholomew's Hospital, German Hospital, London, England **A double-blind controlled study of pimozide versus chlorpromazine in mania.** Psychopharmacology Bulletin. 16(3):38-41, 1980.

In a double-blind controlled study of pimozide versus chlorpromazine in 23 manic patients is described. The finding that manic patients improved in clinical ratings confirms earlier reports of the clinical efficacy of pimozide in mania. Treatment with pimozide was only infrequently associated with obvious sedation, and the improvement in severity of manic symptoms developed smoothly over the course of 2 weeks. By contrast, treatment with chlorpromazine was frequently associated with obvious sedation. Results are compatible with the hypothesis that certain manic symptoms represent an overactivity of dopaminergic pathways in the brain.

004479 Coper, Helmut; Fahndrich, Erdmann; Gebert, Alfred; Helmchen, Hanfried; Honecker, Henning; Muller-Oerlinghausen, Bruno; Pietzcker, Adolf. Fahndrich: Psychiatrische Klinik der Freien Univ. Berlin, Nussbaumallee 36, D-1000 Berlin 19, Germany **Depression and monoamine oxidase.** Progress in Neuro-Psychopharmacology. 3(5/6):441-463, 1979.

Methodological problems in the research literature investigating the relationship between depression and monoamine oxidase (MAO) are identified, and results of a methodologically improved study of MAO activity in depression are described. Pharmacokinetic parameters of platelet MAO activity were determined in 35 psychiatric patients and 25 healthy control Ss (20 endogenous depression, 10 neurotic depression, and 5 manic patients) during and after recovery from the depressive or manic episode using three substrates (tyramine, tryptamine, and phenylethylamine). Results show no differences between the characteristics of platelet MAO in depressive or manic patients and those of normal Ss. Furthermore, treatment with tricyclic antidepressants had no effect on MAO activity. 42 references. (Author abstract modified)

004480 De Maio, D.; Drago, F.; Nielsen, P.; Ascalone, V.; Cisternino, M. Ospedale Fatebenefratelli, Corso de Porta Nuova, I-20121 Milan, Italy **Plasma concentrations of amitriptyline during single nightly and thrice daily administration: cross-over study.** Arzneimittel-Forschung. 30(2)335-337, 1980.

Plasma amitriptyline and nortriptyline concentrations were measured in 10 depressed inpatients after administration of amitriptyline hydrochloride 75mg in three divided doses or as a single nightly does. Mean steady state plasma concentrations during the two dosage regimens were similar. Plasma level differences between dosage schedules at sampling times were small and not significant. It is concluded that the single nightly administration of amitriptyline is a helpful therapeutic schedule which can be used instead of the divided dose when the opportunity is given. 12 references. (Author abstract modified)

004481 Donlon, Patrick T. University of Californiaat Davis, Sacramento, CA 95817 **Factors influencing clinical response to psychotropic drugs: imipramine in depression.** International Pharmacopsychiatry. 14(3):135-148, 1979.

Factors that can influence the clinical response to psychotropic drugs are discussed, with emphasis on imipramine and other tricyclic antidepressants. These factors include pharmacodynamics, bioavailability, and tissue sensitivity; placebo response; compliance and adverse effects; and concurrent life events, illness, and treatment. The importance of proper diagnosis and evaluation of outcome are considered. 49 references. (Author abstract modified)

004482 Dorman, T. Pastures Hospital, Mickleover, Derby, England **Clinical trial comparison of a sustained release form of amitriptyline with dothiepin.** Journal of International Medical Research. 8(4):286-292, 1980.

A double-blind between-group trial was undertaken in 50 depressed patients to compare the efficacy of a sustained release form of amitriptyline (Lentizol) with dothiepin (Prothiaden) over a 5 week period. Patients fulfilling defined admission criteria were randomly allocated to treatment with evening dosage of either 50 mg of the sustained release preparation or 75 mg of dothiepin for the first week of the trial. Subject to review as necessary, these dosages were double at the end of the first week. Both drugs effected significant and appreciable improvement over the 5 week period, with the mean responses at the end of the trial retaining the same relative positions as at the beginning. 12 references. (Author abstract)

004483 Dotti, Andrea; Bernini, Patrizio. Istituto di Clinica Psichiatrica, Universita di Roma, Rome, Italy **/Catamnestic research on reasons for interrupting continuation therapy with lithium carbonate./** Indagine catamnestica sulle ragioni dell'interruzione della terapia continuativa con carbonato di litio. Rivista di Psichiatria. 14(4):293-307, 1979.

Reasons for interruption of therapy using lithium carbonate were studied. A sample of 201 patients was treated for 3 years with lithium salts to prevent manic-depressive relapses. Of the 201 subjects, 67 interrupted the therapy. Results inferred from

data analysis and direct interviews indicate that in a great number of cases the interruption was only apparent, that in many cases there had not been a correct therapeutic indication, and that collateral effects did not significantly affect the interruption. The possibility that lithium can have negative effects on cognitive function is indicated. It is concluded that the preventive efficacy of lithium was not demonstrated in this study since 11 subjects relapsed after the suspension of lithium. 21 references. (Journal abstract modified)

004484 Elizur, A.; Wintner, I.; Davidson, S. Shalvata Psychiatric Center, Sackler School of Medicine, Tel Aviv University, P.O.B. 94, Hod Hasharon, Israel **The clinical and psychological effects of pemoline in depressed patients -- a controlled study.** International Pharmacopsychiatry. 14(3):127-134, 1979.

The clinical and psychological effects of pemoline (50mg/day) were compared with placebo in a 3 week double-blind study of 20 depressed patients. Target symptoms were disturbances of concentration and memory, tension, depression, fatigue, decreased libido, anorexia, and insomnia. The two groups were matched for clinical picture, age, sex, and duration of illness. Comparison of the placebo and pemoline groups on the Modified Hamilton Rating Scale showed significant improvement in concentration and memory, and relief from tension, depression, and fatigue for the drug group. However, no significant differences were found between groups in the Clinical Global Impression or on psychological tests administered at the beginning and end of the study. 12 references. (Author abstract modified)

004485 Engel-Sittenfeld, Pola; Grona, Reinhard; Greil, Waldemar; Jungkunz, Gert. Abteilung fur Experimentelle und Klinische Psych. der Psychiatrischen Klinik der Universitat, Nussbaumstrasse 7, D-8000 Munich 2, Germany **Group behavior therapy as an additional treatment to the lithium prophylaxis of affective psychosis.** Behavioural Analysis and Modification. 3(4):276-279, 1979.

The effects of group behavior therapy as an additional treatment to the lithium prophylaxis of affective psychosis were examined with 10 endogenous depressive patients. The problem intensity as measured individually through a problem barometer as well as the MMPI reduced significantly over the 10-session treatment. Patient's self-image regarding social resonance improved. It is concluded that in lithium treated patients behavior therapy methods can be used in the modification of typical behavior disorders. 10 references. (Author abstract modified)

004486 Escobar, Javier I.; Gomez, Jaime; Constain, Cesar; Rey, Jorge; Santacruz, Hernan. VA, Neighborhood Center, 915 N. Bonnie Beach Place, East Los Angeles, CA 90063 **Controlled clinical trial with trazodone, a novel antidepressant. A South American experience.** Journal of Clinical Pharmacology. 20(2-3):124-130, 1980.

The efficacy and safety of trazodone for the treatment of depressed patients, diagnosed according to research criteria, was evaluated and compared to imipramine and placebo. The patients were from the inpatient psychiatric unit of the Neurological Institute in Bogota, Columbia. The results indicate that trazodone was not as effective as imipramine in reducing depression. However, trazodone was well tolerated producing significantly fewer adverse effects than imipramine. Although two thirds of trazodone treated patients showed symptomatic improvement, an unusually high placebo response also resulted, which exceeded rates found in the US. It is suggested that this may be the reflection of cultural and pharmacogenetic phenomena. 17 references.

004487 Escobar, Javier I.; Tuason, Vicente B. Dept. of Psychiatry and Pharmacology, University of Tennessee, Memphis, TN **Antidepressant agents -- a cross-cultural study.** Psychopharmacology Bulletin. 16(3):49-52, 1980.

Patients suffering from endogenous depression were treated at two US centers and at a Colombian center as part of a collaborative multicenter effort to evaluate the efficacy and safety of the novel antidepressant trazodone, using imipramine and placebo as comparison drugs. Uniform diagnostic, therapeutic, and evaluative procedures were followed. Results are interpreted as supporting the observation that core symptoms of depression are found across cultures and that cultural elements color the syndrome. In both countries, imipramine showed a consistent superiority over placebo. However, Colombian Ss responded generally better than US Ss regardless of the treatment given. A high rate of suicidal ideation in the Colombian sample is noted. 10 references.

004488 Feighner, John P. 1015 Devonshire Drive, Encinitas, CA 92024 **Trazodone, a triazolopyridine derivative, in primary depressive disorder.** Journal of Clinical Psychiatry. 41(7):250-255, 1980.

The effects of imipramine and placebo were compared with trazodone, a new antidepressant, in 45 hospitalized patients with primary depression. A double-blind design was used and after a 3 to 7 day baseline period, patients were treated for 4 weeks. Response was assessed by the Hamilton Psychiatric Scale for Depression, Structured Clinical Interview, Clinical Global Impression, and Global Ward Behavior Scale. The antidepressant effect of trazodone was evident within 7 days of treatment and persisted throughout. Patients treated with imipramine also improved, but the response was not as great or as rapid as in the trazodone group. 16 references. (Author abstract modified)

004489 Feighner, John P.; Brauzer, Benjamin; Gelenberg, Alan J.; Gomez, Evaristo; Kiev, Ari; Kurland, Morton L.; Weiss, Brian L. Psychiatric Centers at San Diego Medical Group, Inc., P.O. Box 1660, La Mesa, CA 92041 **A placebo-controlled multicenter trial of limbitrol versus its components (amitriptyline and chlordiazepoxide) in the symptomatic treatment of depressive illness.** Psychopharmacology. 61(2):217-225, 1979.

In a multicenter, placebo controlled clinical trial, the efficacy in primary depression of limbitrol was compared with that of its components, amitriptyline and chlordiazepoxide. A total of 279 patients with a diagnosis of primary depression was evaluated with the Hamilton depression scale, the Beck depression inventory, and physician and patient global change measures. Significant differences favoring limbitrol occurred after 1 week of treatment, and a trend in favor of limbitrol continued throughout the remaining 3 weeks. In most efficacy comparisons, the combination was as good as, or better than, amitriptyline alone. It was superior to chlordiazepoxide alone after 2 and 4 weeks of treatment. Each component produced an independent contribution to the total therapeutic effect: the chlordizaepoxide effect was more prominent in the first 2 weeks and the amitriptyline effect in the latter 2 weeks. A trend favoring amitriptyline over chlordiazepoxide was evident by week 4. The overall incidence of side-effcts was comparable in both limbitrol and amitriptyline treated groups. Limbitrol treated patients exhibited more sedation, but significantly fewer limbitrol patients deiscontinued treatment prematurely because of side-effects. 13 references. (Author abstract modified)

004490 Feldmann, Harry S.; Denber, Herman C. B. 15, Avenue Krieg, CH-1208 Geneva, Switzerland **Fluotracen (SKF 28, 175): a new antidepressant. Double-blind study with amitriptyline.** Progress in Neuro-Psychopharmacology. 4(1):51-56, 1980.

A double-blind study of a new antidepressant, fluotracen (SKF 28, 175), and amitriptyline in 30 private practice outpatients with symptoms of depression is described. Fluotracen was found to be a rapidly acting antidepressant, with clinical effects apparent often in 4 days (mean effective dosage equals 100mg/day). The maximum dosage employed was 200mg/day, and side-effects were minimal. It is conclued that this compound warrants further investigation on a much larger sample and that this drug will probably represent a second generation of antidepressants where rapidity of onset of action and minimum toxicity are desired. 3 references. (Author abstract modified)

004491 Floru, L.; Tegeler, J. Rheinische Landesklinik, Psychiatrische Klinik der Universitat Dusseldorf, Berg. Landstrasse 2, D-4000 Dusseldorf 12, Germany **/A comparative study of the antidepressives viloxazine and imipramine./** Ein vergleichende Untersuchung der beiden Antidepressiva Viloxazin und Imipramin. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(4):313-320, 1980.

The drug profiles and side-effects of viloxazine and imipramine were compared in a double-blind study of 50 female patients with involutional or endogenous depressions. Subjects received 50 mg oral viloxazine or 25 mg oral imipramine during the first 7 days of treatment and doses were doubled during the following 3 weeks. The AMP system was used to evaluate somatic and psychopathological state; a seven factor self-rating instrument was also used. In the imipramine group, the rate of dropouts was significantly higher due to confused states. Viloxazine appeared to have a more rapid onset of action than imipramine (5th to 8th day of treatment versus 8th to 10th day). Analysis of variance of the four AMP depressive syndromes and of the factors of the self-rating scale did not reveal any significant differences between the two antidepressive drugs. Anticholinergic side-effects such as dryness of the mouth, disturbances of accommodation, sweating, tremor, and unpleasant cardiac sensations were less pronounced and less frequent with viloxazine. There was no difference for nausea and vomiting for the two drug regimes. The low incidence of anticholinergic effects, blood pressure decrease, and ECG abnormalities makes volxazine particularly useful in the treatment of the elderly or others prone to side-effects. 30 references. (Journal abstract modified)

004492 Gerner, R.; Estabrook, W.; Steuer, J.; Jarvik, L. Dept. of Psychiatry, Neuropsychiatric Institute, 760 Westwood Plaza, Los Angeles, CA 90024 **Treatment of geriatric depression with trazodone, imipramine, and placebo: a double-blind study.** Journal of Clinical Psychology. 41(6):216-220, 1980.

Sixty unipolar depressed geriatric outpatients were subjects in a double-blind study of a new antidepressant, trazodone, versus imipramine and placebo. Over the 4 week study, patients in the two active medication groups improved significantly compared to placebo on both observer and self-ratings. Although imipramine and trazodone had similar therapeutic efficacy, trazodone was judged to have fewer side-effects than imipramine. It is suggested that trazodone may have particular clinical utility in the geriatric population which is especially vulnerable to cardiovascular and anticholinergic side-effects. 38 references. (Author abstract)

004493 Gillis, John S.; Moran, Thomas J. Oregon State University, Corvallis, OR 97331 **The effects of amitriptyline and imipramine on interpersonal learning with depressed patients.** Research Communications in Psychology, Psychiatry, and Behavior. 5(2):157-175, 1980.

The effects of two commonly used tricyclic antidepressants, amitriptyline and imipramine, were assessed on several parameters of interpersonal learning with 30 depressed patients. Performance was compared on a series of indices derived from the learning measures. While no differences among treatments reached traditional levels of significance, there was a highly consistent pattern of nonsignificant differences. Results indicate amitriptyline subjects performed best on every major index of interpersonal learning. 18 references. (Author abstract modified)

004494 Goldberg, Harold M.; Finnerty, Richard J. West-Ros-Park Mental Health Center, Hyde Park, MA **A double-blind study of trazodone.** Psychopharmacology Bulletin. 16(3):47-49, 1980.

Results of a double-blind, parallel comparison of trazodone, amitriptyline, and placebo in outpatients with neurotic depression are presented. Physicians' overall evaluation of therapeutic effect at the conclusion of the study was available for 114 of the 127 patients evaluated for drug efficacy. Moderate to marked improvement was noted in 53% of the placebo treatment patients, 70.5% of the amitriptyline treated patients, and 81% of the trazodone treated patients. Safety was evaluated in all patients on the basis of vital signs, laboratory studies, and side-effects. Based on the results, trazodone, a phenylpiperazine derivative of triazolopyridine, appears to be a valuable agent for the relief of symptoms of neurotic depression with associated anxiety.

004495 Goldner, Richard D. 705 Adams, Saginaw, MI 48602 **Clinical observations on scopolamine-ECT and scopolamine-flurothyl for treatment of depressions in private practice.** Journal of Altered States of Consciousness. 5(4):339-349, 1980.

Results of an uncontrolled study of flurothyl convulsive therapy (FCT) or electroconvulsive therapy (ECT) applied to 52 severely depressed patients (including endogenous depressive neurosis, manic-depression, psychotic depression, agitated depression, and involutional melacholia) during scopolamine sleep treatment are reported. Results favored the concept of supramaximal seizure with greater therapeutic power than standard convulsive therapy. Four or five combined scopolamine/ECT treatments appeared equal to double that number of the usual type. Delirium was readily produced by closely spaced FCT or ECT and appeared of therapeutic benefit. One patient developed cerebral thrombosis after completion of somatic therapy; serious complications occurred during active somatic therapy. Scopolamine/ECT, the surviving method since flurothyl is no longer available, is advised for treatment of serious refractory depressions by a physician experienced with atropine toxicity or scopolamine sleep treatment. 10 references. (Author abstract modified)

004496 Guensberger, E.; Molcan, J.; Caplova, T.; Fleischer, J. Psychiatric Clinic, University of Bratis, Bratislava **/Planning the treatment of depressive states with psychotropic drugs./** Strategie der Therapie depressiver Zustande mit Psychopharmaka. Agressologie. 20(D):315-318, 1979.

A number of guiding principles to be adopted in planning the treatment of depressive states with psychotropic drugs are outlined. A close look is taken at the present state and developments in the treatment of depression, illustrated by a previously described method for the continuous monitoring of depressive states by the recording of anxiety, depression, and hypobulia. This method provides a more than one dimensional clinical picture, so that methods to combat depression can be taken, depending on the phase and development of the condition and the response to previous treatment. Case studies are presented in which continuous monitoring of depressive states was employed. 5 references. (Journal abstract modified)

004497 Halaris, Angelos E.; Demet, Edward M. Dept. of Psychiatry, University of Chicago, 950 East 59th St., Chicago, IL

60637 **Open trial evaluation of a pyrrolidine derivative (AHR-1118) on norepinephrine metabolism.** Progress in Neuro-Psychopharmacology. 4(1):43-49, 1980.

The effect of AHR-1118, a nontricyclic antidepressant, on plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) was evaluated in depressive patients. Seven inpatients suffering from primary major depressive disorder participated in the study designed as an open trial. AHR-1118 caused significant and time dependent changes in plasma levels of MHPG. Levels increased several fold at the second week of treatment and returned to baseline at the end of the fourth week. Clinical improvement (measured with the Hamilton Depression Scale and the Zung Self-rating Scale for Depression) occurred in phases as did the changes in plasma MHPG. Significant correlations were obtained between the rate of clinical improvement and the biochemical changes. It is concluded that reuptake blockade of norepinephrine by the pyrrolidine derivative AHR-1118 produces changes that are reflected in plasma MHPG levels. 8 references. (Author abstract modifed)

004498 Hansen, L. Bolvig; Thomsen, I. Scheel; Vestergard, P.; Larsen, N. E.; Hvidberg, E. F. Dept. R, Mental Hospital Nordvang, DK-2600 Glostrup, Denmark **Plasma levels of zimelidine and norzimelidine in endogenous depression.** Psycopharmacology. 69(2):157-160, 1980.

A new serotonin uptake inhibitor zimelidine was studied in 16 endogenously depressed inpatients, who received 150mg/day orally during 3 to 6 weeks in a phase II type study. Plasma concentrations of zimelidine and its main metabolite norzimelidine were determined twice a week. Ten patients obtained a well defined steady-state plasma level within 1 to 2 weeks, while three patients still had increasing concentrations of both substances or only norzimelidine within the investigation period. In two patients, biochemical affection of the liver could be demonstrated during the treatment; one associated with moderate clinical symptoms (dizziness and fever), the other without clinical symptoms. Both patients recovered upon cessation of the zimelidine treatment. In the former patient, very high concentrations of zimelidine at the time of hepatic symptoms were demonstrated, while the latter patient was within the average concentration range. Other adverse reactions were mild and few, particularly with respect to anticholinergic effects. With the applied, probably suboptimal, dosage the therapeutic response was only satisfactory in five cases. 13 references. (Author abstract modified)

004499 Herceg-Baron, Roberta L.; Prusoff, Brigitte A.; Weissman, Myrna M.; DiMascio, Alberto; Neu, Carlos; Klerman, Gerald L. Yale University School of Medicine, Dept. of Psychiatry, 904 Howard Ave., Suite 2A, New Haven, CT 06519 **Pharmacotherapy and psychotherapy in acutely depressed patients: a study of attrition patterns in a clinical trial.** Comprehensive Psychiatry. 20(4):315-325, 1979.

To examine the relationship between patient attrition and the efficacy, safety, and feasibility of a treatment, the attrition patterns of acutely depressed patients assigned to one of four clinical trials were monitored. The four clinical modes were: psychotherapy; pharmacotherapy; both treatments taken together; and nonscheduled treatment. Data show that patients offered psychotherapy initially refused unless they were also given pharmacotherapy. Patients given pharmacotherapy initially accepted the treatment but tended to withdraw for both symptomatic and nonsymptomatic reasons. Patients offered the nonscheduled therapy initially accepted the treatment, but did not tolerate it well. Results lend further support to the efficacy of combination treatment. 12 references.

004500 Hirschfeld, R. M. A.; Klerman, Gerald L. Depression Section, Clinical Research Branch, NIMH, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857 **Treatment of depression in the elderly.** Geriatrics. 34(10):51-57, 1979.

Evaluation of the depressed elderly patient, characteristics of clinical depression and senile dementia, drugs associated with depression, drugs used in treating depressions, and drugs affecting the actions of antidepressants are discussed. Since depression in the elderly may be secondary to malignancies, endocrine disturbances, and metabolic problems, a careful physical and laboratory evaluation of the depressed elderly patient is essential. The management problems associated with depression in the elderly and the necessity of determining both the suicide risk and the need for hospitalization are discussed. 9 references.

004501 Johnston, B. B.; Naylor, G. J.; Dick, E. G.; Hopwood, S. E.; Dick, D. A. T. Stratheden Hospital, Cupar, Fife, Scotland **Prediction of clinical course of bipolar manic depressive illness treated with lithium.** Psychological Medicine. 10(2):329-334, 1980.

A group of 44 bipolar manic depressive patients attending a routine lithium clinic were investigated. The results suggest that when on treatment with lithium, manic-depressive patients with a good prognosis tend to have a higher erythrocyte Na-K ATPase and higher plasma and erythrocyte lithium concentrations than those with a poor prognosis. There was no evidence to suggest that the erythrocyte/plasma lithium ratio was useful in predicting clinical response to lithium therapy. There was also a positive correlation between plasma lithium concentration and Na-K ATPase activity, confirming that in manic-depressive subjects lithium produces a rise in erythrocyte Na-K ATPase activity. 15 references. (Author abstract)

004502 Krysa, Grazyna; Pacyna, Maria; Pietruszewska, Irena; Stencka, Krystyna. Klinika Psychiatryczna AM, ul. Nowowiejska 27, 00-665 Warsaw, Poland /**Analysis of the problem of conducting biochemical studies in depressive patients based on the study of disintegration products of biogenic amines in the urine.**/ Analiza trudnosci prowadzenia badan biochemicznych u chorych depresyjnych na podstawie oznaczania w moczu produktow rozpadu amin biogennych. Psychiatria Polska. 14(1):11-18, 1980.

A study investigating the excretion of homovanillic (HVA), vanillylmandelic (VMA), and 5-hydroxyindoleacetic (5-HIAA) acids and kinurenine in the urine of 52 patients with various depressive syndromes and in 10 normal volunteers is presented. An analysis was made concerning the methodological difficulties of conducting biochemical studies in an open psychiatric ward. It was found that: 1) there was no difference in HVA, VMA, 5-HIAA and kinurenine excretion between patients with the depressive syndrome and the control subjects; 2) the VMA level was significantly higher in patients who had received psychotropic drugs sporadically than in patients who had received no medication. In addition, the level of metabolite excretion in that group did not change after further treatment; and 3) the group of patients who had received no medication during the 2-3 days preceding the first examination but who had previously received pharmacological treatment were characterized by low values of HVA and 5-HIAA excretion. It is also indicated that further pharmacological therapy conducted in the hospital for over 3 weeks brought about a significant increase in HVA excretion. 30 references. (Journal abstract modified)

004503 Kuhne, G.-E.; Walther, H.; Kohler, E.; Grunes, J.-U. Nervenklinik der Medizinischen, Akademie Magdeburg, Leipziger Str. 44, DDR-301 Magdeburg, Germany /**Activity profile of the blood level with administration of Thioridazine.**/

Blutspiegelwirkungsprofil bei Thioridazin. Agressologie. 20(D):271-274, 1979.

The blood levels of 10 patients with dysthymic depression were studied following administration of thioridazine. It was found that: 1) there were considerable differences in the steady state blood level values between different individuals; 2) psychological and psychopathological estimates indicated a continuous improvement in test scores with administration of thioridazine;) the fall in the plasma concentration during the observation period was clealy evident and applied both to the morning and afternoon self values, possible reflecting a spontaneous induction of thioridazine metabolism; and 4) constant circadian variations were observed, which were reflected in lower midday values. An improvement in test score was obtained in patients with higher than average blood levels but not in the group with low blood levels, indicating a probable connection between blood level and improvement in the test score. 12 references. (Journal abstract modified)

004504 Kupfer, D. J.; Spiker, D. G.; Coble, P.; Neil, J. F.; Hanin, I.; Edwards, D. J.; McPartland, R. J.; Shaw, D. H.; Holzer, B. Department of Psychiatry, University of Pittsburgh, School of Medicine, Pittsburgh, PA 15261 **EEG sleep and affective disorders: what can it predict?** In: Usdin, E., Catecholamines: basic and clinical frontiers. Elmsford, Pergamon, 1979. 947 p. Vol. 2. (p. 1920-1922).

In patients with primary depression, early EEG changes in response to amitriptyline were highly correlated with the final clinical response to the drug 4 weeks after initial administration. These immediate changes included rapid REM suppression (43%) and prolongation of REM latency (187%), suggesting an initial alteration in multitransmitter levels that may be related to eventual clinical change. Since catecholaminergic and cholinergic neurons have been implicated in the control and intensity of REM sleep, a more active search for REM sleep/tricyclic drug mechanisms is warranted. 5 references. (Author abstract modified)

004505 Kupfer, David J.; Coble, Patricia A.; Rubinstein, Debra. Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15261 **Changes in weight during treatment for depression.** Psychosomatic Medicine. 41(7):535-544, 1979.

Changes in appetite and weight were examined in a group of 47 carefully diagnosed primary depressives who were treated in a random design with either placebo or amitriptyline over a 35 day protocol. While the amitriptyline treated group showed a greater gain in weight than did the placebo group, no differential effects could be demonstrated between drug responders and nonresponders. There was a relationship between the report of decreased appetite and clinical severity of depression in the drug nonresponder subgroup despite significant weight gain during the protocol. Thus, weight change during this study period did not appear to show a simple relationship to corresponding clinical change. The clinical lore that has supported the notion that increased appetite and weight gain in patients being treated with tricyclic antidepressants are good signs cannot be confirmed by the findings. 14 references. (Author abstract modified)

004506 Lavagna, J.; Capdeville, C.; Myquel, M.; Braccini, T.; Vernet, J. P.; Orth, J.-P.; Darcourt, Guy. Service de Psychiatrie et de Psychologie Medicale du C.H.U. de Nice, Hopital Pasteur, F-06031 Nice, France **/Treatment of depressive states with nortriptyline./** Traitement des depressions par la nortriptyline. Psychologie Medicale. 11(1):201-210, 1979.

A daily dose of 150mg of nortriptyline was given to 37 patients hospitalized for depressive states of various types to test the antidepressive effect of the drug. The Hamilton and Zerssen scales were used to evaluate the intensity of the depression. The antidepressive action of the drug was registered by the improvements in the scores of the two scales. The side-effects observed were those that emerge in tricyclic antidepressants. Anxiety, psychostimulant action, and insomnia which sometimes appeared led to the conclusion that the drug operated as a psychostimulant. The tolerance was found to be excellent. 12 references. (Journal abstract modified)

004507 Lipper, Steven; Murphy, Dennis L.; Slater, Stanley; Buchsbaum, Monte S. NIH Clinical Center, 10-3D48, Bethesda, MD 20205 **Comparative behavioral effects of clorgyline and pargyline in man: a preliminary evaluation.** Psychopharmacology. 62(2):123-128, 1979.

The antidepressant and other behavioral effects of clorgyline, a preferential inhibitor of monoamine oxidase (MAO) type-A, were compared with those of pargyline, a preferential inhibitor of MAO type-B, in 16 depressed patients. In a subgroup of more severely depressed patients, clorgyline treatment for 4 weeks resulted in significant improvement on both observer rated and self-rated scales, while minimal changes occurred during pargyline treatment. Similarly, in a crossover study that included eight patients examined with multiple scales, clorgyline had generally greater antidepressant and antianxiety effects than did pargyline, although pargyline had some activating effects and also tended to produce more side-effects. MAO type-A inhibition may be more important than MAO type-B inhibition for antidepressant efficacy. 26 references. (Author abstract)

004508 Maas, James W. Dept. of Psychiatry, Yale University School of Medicine, New Haven, CT 06510 **Neurotransmitters and depression: too much, too little, or too unstable?** Trends in NeuroSciences. 2(12):306-308, 1979.

The literature on the measurement of levels of brain neurotransmitter concentrations and metabolism and the effects of antidepressant treatment on these levels is reviewed. In addition, a model of the functioning of neurotransmitter systems in affective disorders which posits that affective disorders result from conditions of neurotransmitter is described. Confusing issues or apparent contradictions in the literature are discussed in terms of the model. 17 references. (Author abstract modified)

004509 McNair, Douglas M.; Czerlinsky, Thomas; Kahn, Richard J.; Fisher, Seymour. Division of Psychiatry, Boston University School of Medicine, Boston, MA **An anxiolytic drug trial with student patients and student symptomatic volunteers.** Psychopharmacology Bulletin. 16(3):27-29, 1980.

Preliminary results of an anxiolytic drug trial (chlordiazepoxide and placebo) with student patients and student symptomatic volunteers are described. Patients and volunteers exceeded specified minimum scores on the anxiety factors of the Profile of Mood States (POMS) and the Hopkins Symptom Checklist (HSCL) and met other typical criteria. Three significant group differences indicated that student volunteers: (1) had a longer current episode; (2) were younger at first episode; and (3) had situational factors rated by psychiatrists as being less important in their current episode. An analysis of main effects after 1 and 4 weeks of treatment showed numerous drug effects, but no simple group effects or effects of traditionalism (Bass Acquiescence Scale). All dependent measures indicated that placebo yielded greater improvement than chlordiazepoxide for depressive symptomatology. 4 references.

004510 Medvecky, J.; Medvecka, E. Psychiatric Clinic, Faculty Hospital, Kosice, Czechoslovakia **/Administration of Noveril in cases of depression./** Noveril bei der Depressionen. Agressologie. (20)D:311-313, 1979.

The effects of the Noveril the antidepressant dibenzepine on depressed patients were studied. Subjects were 20 patients suffering from depressive states of different etiology, predominantly states of involutional melancholia. The preparation was administered orally in doses of 360mg to 720mg daily. The anxiolytic effect predominated during the initial states of treatment, whereas the effect on depression only became apparent after a longer period of treatment. The good tolerance and only minor anticholinergic action of Noveril were striking. No changes were observed in primary biochemical indices or in ECG. The administration of Noveril to patients suffering from glaucoma and cardiac insufficiency caused no deterioration in the physical condition. Very good results were obtained in 6 patients and good results in 11 patients. A combined electroconvulsive treatment was required in two cases, and the treatment was ineffective in one case. (Journal abstract modified)

004511 Michalewski, Henry J.; Thompson, Larry W.; Patterson, Julie V. Dept. of Psychology, University of Southern California, Los Angeles, CA **Brain amine hypothesis.** Psychopharmacology Bulletin. 16(2):16-18, 1980.

Clinical and experimental studies dealing with the role of biogenic amines in the pathogenesis of affective illnesses is reviewed, and the brain amine hypothesis is evaluated. Topics discussed include: the role of monoamine oxidase (MAO) activity in the etiology of depressive illness; the hypothesized potentiation of the physiological effects of norepinephrine and serotonin by the tricyclic antidepressant drugs; the effects of tricyclic antidepressant drugs on the reuptake of serotonin; the hypothesized mechanism of action of the increase in available norepinephrine, dopamine, and serotonin caused by MAO inhibitors; and a hypothesized reduced availability of central catecholamines with aging. 16 references.

004512 Milln, Philip; Coppen, Alec. MRC Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **Who responds to amitriptyline?** Lancet. No. 8171:763-764, 1980.

The effects of amitriptyline on patients with unipolar primary depression were tested. The patients were divided on the basis of family history; familial pure depressive disease (FPDD) in which there is a positive family history of depression in first degree relations but no family history of mania, alcoholism or antisocial personality, and sporadic depressive disease (SDD) which is depression in an individual with no history of psychiatric illness in first degree relations. Patients were treated with 150mg amitriptyline daily for 6 weeks. The results indicated that only patients with FPDD and with a Newcastle scale score in the 4 to 8 range showed a substantial improvement with amitriptyline. 13 references.

004513 Moreira, Mario Santos. Av. Princesa Isabel, 150, s/404, 22011 Rio de Janeiro, Brazil **/Clinical trial comparing lofepramine with amitriptyline chlordiazepoxide in treatment of depression./** Avaliacao terapeutica da lofepramina em estudo comparativco com amitriptilina clordiazepoxido no tratamento da depressao. Jornal Brasileiro de Psiquiatria. 29(3):203-209, 1980.

The therapeutic efficacy and tolerance of lofepramine for treating depression was studied. A double-blind group comparative trial was carried out involving 50 patients suffering from slight, moderate or severe depression. These patients were randomly allocated into two groups with equal number of cases: an experimental group treated with lofepramine (3 x 35mg/day) and a control group treated with amitriptyline plus chlordiazepoxide (3 x 12.5mg plus 5mg/day); both for a duration of 6 weeks. Results were evaluated according to the Hamilton Depression Scale. Results indicate that both treatments were very active without any statistically significant difference between the two drugs. Lofepramine was efficacious in the treatment of several forms of depression including somatization and anxiety. Side-effects were minimal. 7 references. (Journal abstract modified)

004514 Muller, Oerlinghausen, B.; Ruther, E.; Adam, H. K.; Bente, D.; Busch, H.; Fahndrich, E.; Greil, W.; Jungkunz, G.; Kuss, H.-J. Psychiatrische Klinik, Freie Universitat Berlin, Nussbaum-Allee 36, D-1000 Berlin 19, Germany **Clinical profiles and serum concentration of viloxazine as compared to amitriptyline.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(4):321-337, 1980.

The clinical profile and serum concentration of viloxazine (300 mg/d) and amitriptyline (150 mg/d) were compared in a 3 week double-blind trial in 41 patients with depressive syndromes. Psychopathological changes were documented by means of the Hamilton Depression Rating scale (HDRS), the Bf-S (Zerssen), the AMDP diagnostic system, and videotaped recordings. In addition to routine clinical chemical tests, drug serum concentrations were monitored. The number of global responders and nonresponders, defined according to final HDRS scores, was equally distributed between the two drug groups. The AMDP evaluation suggested that viloxazine had a somewhat more marked and rapid effect on symptoms of retardation, whereas amitriptyline acted predominantly on depressive mood, sleep disturbances, and vital feelings. The EEG profile of both drugs was similar to the spectral changes seen under tricyclic antidepressants, although only viloxazine-induced changes reached statistical significance on the 10th and 20th day, the variability of EEG recordings was greater in the amitriptyline group. Viloxazine blood levels showed a remarkably low interindividual and intraindividual variance. Steady state was reached at day 5 at the latest. Amitriptyline serum concentrations still increased between the 10th and 21st day. The average blood concentration of viloxazine was higher in the responder than in the nonresponder group. 42 references. (Author abstract modified)

004515 Nash, Ralph J. Clinical Research Psychopharmacology, Hoechst-Roussel Pharmaceuticals, Inc., Somerville, NJ **Overview of nomifensine maleate antidepressant studies in the U.S.** Psychopharmacology Bulletin. 16(3):46-47, 1980.

A brief overview of 18 double-blind, randomized treatment, parallel group, block design studies comparing nomifensine maleate with either placebo alone, imipramine alone, or with placebo and amipramine is presented. The results are consistent in demonstrating nomifensine's superiority over placebo and show that this drug is at least equivalent in its effect to the standard reference drug, imipramine HCl. As judged by the investigators, approximately two thirds of patients in both active medication groups showed marked or moderate improvement. Although side-effects occurred in some patients treated with nominfensine, they had a much higher incidence in patients treated with imipramine HCl. In reports of overdoses of nomifensine of up to 3.5g, no apparent cardiotoxic effects or other important medical sequelae were observed.

004516 Post, Robert M.; Ballenger, James C.; Hare, Theodore A.; Bunney, William E., Jr. NIMH, Bldg. 10, Bethesda, MD 20205 **Lack of effect of carbamazepine on gamma-aminobutyric acid in cerebrospinal fluid.** Neurology. 30(9):1008-1011, 1980.

Carbamazepine did not alter GABA levels in the cerebrospinal fluid of nine patients with manic-depressive disorder. The patients were treated with 600 to 1600mg/day for 30 days, achieving blood levels of 6 to 11mcg/ml carbamazepine. These results do not support the suggestion that the anticonvulsant and

psychotropic effects of carbamazepine are due to actions on brain GABA. 33 references. (Author abstract modified)

004517 Puzynski, S.; Bidzinski, A.; Hauptmann, M.; Rode, A.; Jakimow-Venulet, B.; Zaluska, M. Psychoneurological Institute, 1/9 Sobieskiego Str., 02-957 Warsaw, Poland **Peripheral metabolism of indoleamines and catecholamines in endogenous depressive syndrome.** Agressologie. 20(D):245-251, 1979.

Biochemical parameters of indoleamines and catecholamines in the urine and the blood were measured in 18 normal controls and 16 bipolar affective patients. Changes in the parameters were followed in eight depressive patients during treatment with amitryptyline. Affective patients, regardless of their current mental status, seemed to excrete lower amounts of amines and their metabolites in urine than controls. When only patients who were actually in the depressive phase of the illness were compared to the controls, two statistically significant differences between the groups were revealed: a lowered level of urinary 5-HIAA and elevated serotonin in the plasma of depressives. A 3 to 4 week treatment with amitryptyline caused differential changes in the excretion of catecholamines and their metabolites and, in general, seemed to increase the intensity of tryptophan utilization. These changes, however, did not necessarily correlate with the final outcome of treatment. The most noteworthy were the changes in free to bound tryptophan ratio which rose in the patients who improved upon treatment. The results suggest that disturbances in tryptophan distribution and utilization are indeed of importance in the bipolar form of affective illness. 31 references. (Author abstract modified)

004518 Ravaris, C. Lewis; Robinson, Donald S.; Ives, John O.; Nies, Alexander; Bartlett, Diantha. Dept. of Psychiatry, East Carolina University School of Medicine, Greenville, NC 27834 **Phenelzine and amitriptyline in the treatment of depression: a comparison of present and past studies.** Archives of General Psychiatry. 37(9):1075-1080, 1980.

The results of a direct comparison of phenelzine sulfate and amitriptyline hydrochloride therapy in 105 depressed patients are presented. This is probably the first definitive double-blind controlled clinical trial of a monoamine oxidase inhibitor and a tricyclic antidepressnat in the outpatient setting. The results show both antidepressants to be effective, with the similarities between the two exceeding the differences. Both drugs had marked antidepressant and antianxiety effects. Phenelzine tended to exert a stronger antianxiety action; amitriptyline was more effective in reversing weight loss and improving sleep. The incidence of two side-effects, sedation and orthostatic hypotension, was almost identical. Dry mouth was more prevalent with amitriptyline. The indications for the differential clinical use of both drugs in depressed outpatients are discussed. 32 references. (Author abstract)

004519 Reus, Victor I.; Targum, Steven D.; Weingartner, Herbert; Post, Robert M. Post: NIH, 9000 Rockville Pike, Building 10, Room 3S239, Bethesda, MD 20205 **Effect of lithium carbonate on memory processes of bipolar affectively ill patients.** Psychopharmacology. 63(1):39-42, 1979.

The effect of long-term lithium carbonate treatment on parameters of immediate, short-term and long-term memory was examined in a group of bipolar affectively ill patients. The lithium treatment group recalled significantly fewer words across trials on a verbal learning task than a group of bipolar affectively ill patients receiving no medication. The ability to consistently recall material for which prior learning had been demonstrated was also decreased and accounted for most of the variance in total number of words recalled. Possible mechanisms of effect are discussed. 28 references. (Author abstract)

004520 Robinson, Marie Kibble. University of Illinois at Chicago Circle. **Social functioning as a measure of the effectiveness of alternative methods for the treatment of depression. (D.S.W. dissertation).** Dissertation Abstracts International. 40(4):2274-A, 1979. Ann Arbor, Univ. Microfilms No. 7923027, 117p., 1979.

The effectiveness of the University of Illinois Affective Disorders Clinic was measured in terms of changes in social functioning in 30 depressed patients receiving chemotherapy alone or in combination with psychotherapy and classified according to the supportiveness of their environments. All patients were found to show improved social functioning following therapeutic intervention; patients receiving psychotherapy in addition to chemotherapy showed no greater gains than those receiving chemotherapy alone. Patients with supportive environments did not function any better in their social roles than those with less support. Findings are discussed in relation to study assumptions about social values and settings. Results suggest that psychotherapy as an adjunct to chemotherapy might be discontinued without risk of loss of positive result. It is also suggested that the clinic might do well to formalize the psychotherapeutic potential of the medication groups. (Journal abstract modified)

004521 Rosier, Y. Clinique Medicale de Champvert, 60-71, rue Benoist-Mary, F-69322 Lyon Cedex 1, France **/The use of amineptine in the treatment of depression./** L'emploi de l'amineptine dans le traitement de la depression. Psychologie Medicale. 11(1):211-223, 1979.

The way in which the antidepressant drug amineptine manifests its effects was studied through the open observation of 40 patients. With this in mind, the drug was always the only one to be administered even when it was obvious that therapy combined with neuroleptics would have improved the results. Based on the analysis of the effects of the drug on anxiety, sleep, libido, awakening, and sedation as well as hypersthenia, amineptine and monoamine oxidase inhibitors were comparably effective. It is concluded that amineptine attenuated and suppressed more recent depressive constructions and allowed the patients to regain their usual means of defense balance. 34 references. (Journal abstract modified)

004522 Schou, M.; Stromgren, E. no address **Origin, prevention and treatment of affective disorders.** London, Academic Press, 1979. 299 p. $20.25.

Research conducted in the Denmark Psychiatric Institute is reviewed as it relates to the origin, prevention and treatment of affective disorders. This research falls into two categories: 1) basic studies of lithium and related biological areas; and 2) genetic, clinical/epidemiological treatment and prevention aspects of primary affective disorders. Progress in lithium psychopharmacology for depression is highlighted over the past 25 years and specific efforts on long-term response, physiological and behavioral side-effects are discussed. Genetic aspects of the unipolar/bipolar dichotomy, the Kraepelian synthesis of the depressions, twin studies supporting unipolar/bipolar dichotomy, and epidemiological aspects of affective psychoses are also presented.

004523 Shimizu, Muneo; Sakaue, Noriyuki; Kaito, Takao; Ikeda, Ryoichi. Dept. of Neuropsychiatry, Tokyo Medical College Hospital, 6-7-1 Nishishinjuku, Tokyo, Japan **Studies on the use of blood lithium concentrations in lithium therapy in Japan.** International Pharmacopsychiatry. 14(3):170-175, 1979.

The relationship between the concentration of lithium in whole blood and plasma was determined in 11 manic-depressive patients 12 hours after the evening dose of lithium carbonate, taken in the form of slow release tablets (Limas). Significant relationships were found between the concentrations of lithium in

blood and in plasma and between daily doses of lithium and lithium concentrations in blood and plasma. Results suggest that under certain conditions the concentration of lithium in a small sample of whole blood may be used to monitor lithium therapy in outpatients. 10 references. (Author abstract modified)

004524 Shopsin, Baron. New York University Medical Center, New York, NY **Psychopharmacology of the lithium ion: long-term drug prophylaxis in the affective disorders. (Unpublished paper).** Final Report, NIMH Grant 2RO1-MH-17436, 1979. 119 p.

Data are presented on: 1) long-term drug prophylaxis of lithium in the affective disorders; 2) a long-term double-blind controlled comparison with lithium in the treatment of premenstrual tension; and 3) lithium in the treatment of tardive dyskinesia. Data also are presented on the four studies dealing with the basic mechanisms of action and side-effects of the lithium ion: 1) a study of sudden cardiac death during lithium carbonate maintenance; 2) a lithium haloperidol interaction study; 3) EKG and echocardiographic changes in patients on long-term lithium maintenance; and 4) intracellular/extracellular lithium, and magnesium calcium levels in affectively ill outpatients. Data are also given on lithium as an immunologic adjuvant and on genetic studies in affective disorders. Findings from a collaborative study with the Ackerman Institute for Family Therapy and demographic analyses of a clinic outpatient population are presented. Data are given on the use of objective measures for: 1) defining research diagnostic criteria in the affective disorders; 2) clinical assessment of patients on long-term drug maintenance; and 3) prediction of drug response.

004525 Silvestrini, B. Research Institute F. Angelini, Viale Amelia, 70, I-00181 Rome, Italy **Trazodone, a new therapeutic and theoretical approach to depression.** Activitas Nervosa Superior. 21(4):301-303, 1979.

Results of a clinical trial of the new antidepressant drug, trazodone, are presented and the novel theoretical approach to depression which underlies trazodone effects is discussed. The 263 patients suffering from endogenous depression responded significantly better to both trazodone and imipramine than to placebo treatment. However, trazodone, unlike most tricylic antidepressants, does not provoke the side-effects typically associated with potentiation of catecholaminergic systems. The trazodone hypothesis postulates that depression is produced by a disturbance in the mechanisms responsible for emotional integration of unpleasant experiences, and that depression is the mental equivalence of a state of pain. 13 references.

004526 Sjoqvist, Folke. National Institute of General Medical Sciences, NIH, Bethesda, MD 20205 **Overview by drug classes -- clinical monitoring of tricyclic antidepressant plasma concentrations.** Psychopharmacology Bulletin. 16(3):21-24, 1980.

Clinical monitoring of tricyclic antidepressant plasma concentration is reviewed. It is noted that despite methodological shortcomings in published studies, most authors agree that monitoring of some tricyclic antidepressants in plasma is useful in patient management under certain premises and for strict indications. However, uncritical application of the concept should be avoided. In drug trials and experimental studies aimed at exploring mechanisms of drug action in man, knowledge of drug plasma concentrations should be as vital to the clinical investigator as knowledge of substrate concentrations is to a biochemist. 12 references.

004527 Smith, Robert C.; Reed, Kenneth; Leelavathi, Doddamane E. Texas Research Institute of Mental Sciences, Texas Medical Center, Houston, TX **Pharmacokinetics and the effects of nortriptyline in geriatric depressed patients.** Psychopharmacology Bulletin. 16(3):54-57, 1980.

The pharmacokinetics and the effects of nortriptyline in geriatric depressed patients were investigated. Preliminary data from 16 geriatric and younger depressed patients suggest that nortriptyline is a safe and effective antidepressant for the treatment of geriatric depressed patients. Plasma and red blood cell levels of nortryptyline were similar in geriatric and younger patients, and the upper limit of the therapeutic window was also similar in the geriatric age group to that previously reported in studies of younger and middle-aged patients. This suggests that similar dosage regiments of nortryptyline can be used in geriatric patients to achieve similar blood levels and therapeutic effects. At plasma levels within or slightly above the therapeutic window, nortryptyline did not have significant pathological effects on the cardiovascular system, despite in some cases, marked preexisting cardiac pathology. 6 references.

004528 Stern, Theodore A.; Anderson, William H. Harvard Medical School, Massachusetts General Hospital, 1 Fruit Street, Boston, MA 02114 **Benztropine prophylaxis of dystonic reactions.** Psychopharmacology. 61(3):261-262, 1979.

Benztropine prophylaxis of dystonic reactions was investigated in 40 acute psychosis patients receiving high potency oral antipsychotic drugs (oral phenothiazines, a butyrophenone or a thioxathene with or without prophylactic use of an antiparkinson agent). Patients were interviewed to determine the incidence of acute dystonia. An elevenfold increase in dystonia was found in patients who received no prophylactic medication. Such prophylaxis appears effective in preventing acute dystonia. 5 references. (Author abstract modified)

004529 Stern, W. C.; Harto-Truax, N. Dept. of Clinical Research, Burroughs Wellcome Co., Research Triangle Park, NC **Two multicenter studies of the antidepressant effects of bupropion HCl versus placebo.** Psychopharmacology Bulletin. 16(3):43-46, 1980.

The results of two multicenter double-blind studies of bupropion HCl vs placebo in hospitalized depressed patients are presented. Bupropion was found to have significantly greater antidepressant activity than placebo. In the study using the higher dose level of the drug (maximum 740mg/day), greater efficacy than placebo was found as early as 8 days of treatment, compared to an onset of 3 weeks in the lower dose (450mg/day) study. The side-effect profile of this drug in both studies was highly similar to that of placebo. 8 references.

004530 Stewart, Jonathan W.; Quitkin, Frederic; Fyer, Abby. Dept. of Psychiatry, Columbia University, New York, NY 10027 **Efficacy of desmethylimipramine in endogenomorphically depressed patients.** Psychopharmacology Bulletin. 16(3):52-54, 1980.

An attempt to distinguish two subtypes of depressed patients (caused by serotonin or norepinephrine deficiencies) via analysis of pharmacological response is described, and the efficacy of desmethylimipramine (DMI) in endogenomorphically depressed patients is discussed. Lack of a sufficient number of patients entering a randomization phase of the study limits implications of the results for the serotonin and norepinephrine biogenic amine hypotheses of depression. However, if the main action of DMI is to block norepinephrine reuptake, the high response rate to DMI found suggests that endogenomorphic depression criteria may select patients with norepinephrine deficiency and patients with indoleamine deficiency. Either group may present with different symptoms, may have a defect correctable by catecholamine manipulation, or may have relatively uncommon symptoms. 11 references.

004531 Svestka, J.; Nahunek, K.; Ceskova, E. Psychiatric Clinic Medical Faculty, University of Brno, Brno, Czechslovakia **Clinical experience with some beta blocking agents and their derivatives in endogenous depressions.** Agressologie. 20(D):295-298, 1979.

The antidepressant effects of trimepranol beta-blocking agents and of viloxazine were tested in open clinical trials. Subjects were 35 and 42 patients, respectively, in the depressive phase of manic-depressive psychosis. Trimepranol achieved full or partial remission with 44% of the subjects and showed the highest efficacy in the anxious, next highest in the atypical, and the lowest in the inhibited forms of depression. Viloxazin was fully or partially effective in 79% of the subjects and showed significantly better results in inhibited depressions than in other types. In the comparison of the antidepressive efficacy of the two drugs, viloxazin showed the higher global effectiveness, especially in inhibited depressions, while trimepranol with the lower total efficacy produced the best results in anxious forms of depression, 7 references. (Author abstract modified)

004532 Traskman, L.; Asberg, M.; Bertilsson, L.; Cronholm, B.; Mellstrom, B.; Neckers, L.; Sjoqvist, F.; Thoren, P.; Tybring, G. Asberg: Dept. of Psychiatry, Karolinska Hospital, S-104 01 Stockholm 60, Sweden **Plasma levels of chlorimipramine and its demethyl metabolite during treatment of depression.** Clinical Pharmacology and Therapeutics. 26(5):600-610, 1979.

The biochemical and antidepressant effects of chlorimipramine (CI) were studied in depressed patients after 3 weeks of treatment. Treatment with CI caused a decrease in the serotonin and norepinephrine metabolites 5-hydroxyindoleacetic acid (5-HIAA) and 4-hydroxy-3-methoxyphenyl glycol (HMPG), but had no effect on the dopamine metabolite homovanillic acid or on tryptophan in cerebrospinal fluid (CSF). Patients with high levels of 5-HIAA in CSF prior to treatment showed a positive correlation between amelioration of depression and plasma levels of the demethyl metabolite of CI (DMCI) as well as a correlation between HMPG alteration and amelioration of depression. In patients with low levels of 5-HIAA in CSF prior to treatment, correlations between plasma levels of CI and DMCI and behavioral improvement were consistently negative and nonsignificant. 36 references. (Author abstract modified)

004533 van Kammen, Daniel P.; van Scheyen, Jan D.; Murphy, Dennis L. NIMH, Building 10, 9000 Rockville Pike, Bethesda, MD 20205 **Platelet monoamine oxidase activity and clomipramine-induced mania in unipolar depressed patients.** Biological Psychiatry. 15(4):565-573, 1980.

During an asymptomatic phase platelet monoamine oxidase (MAO) activity was examined in 28 unipolar patients, eight of whom previously had developed mania during clomipramine treatment for depression. The platelet MAO activity was not lower in these switchers than in 20 unipolar patients who did not become manic during a similar clomipramine treatment. High but nonsignificant correlations were found among platelet MAO activity and age of onset of mania, duration of clomipramine treatment before the switch, and the duration of manic behavior. These clinical variables correlated significantly amongst themselves. The high and normal platelet MAO activities of these patients neither support nor rule out a Bipolar-I diagnosis. It is concluded that these results support the pharmacologic basic of the induction of mania during clomipramine treatment. 20 references. (Author abstract)

004534 van Praag, Herman; de Haan, Sieest. Dept. of Psychiatry, University Hospital Utrecht, Catharijnesingel 101, P.B. 16250, NL-3500 CG Utrecht, The Netherlands **Depression vulnerability and 5-hydroxytryptophan prophylaxis.** Psychiatry Research. 3(1):75-83, 1980.

On the basis of past research suggesting the involvement of a central 5-hydroxytryptamine (5-HT) deficiency as a potential predisposing factor in a subgroup of endogenous depressions, the prophylactic effects of L-5-hydroxytryptophan (L-5HTP) plus carbidopa were examined in 20 patients with recurrent unipolar and bioolar depression responsive to clomipramine. Half the patients received L-5HTP the first year and placebo the second, while for the other half this sequence was reversed. As predicted, L-5HTP was found to reduce relapse rate in vital depressions with both a bipolar and a unipolar course. The effect was most pronounced in patients with persistent disorders of central 5-HT metabolism; this observation, however, requires corroboration. It is noted that L-5HTP prophylaxis is the first aimed (i.e., pathological substrate oriented) type of chemotherapy known in psychiatry. 38 references. (Author abstract modified)

004535 Zisook, Sidney; Hall, Richard C. W.; Gammon, Elizabeth. Dept. of Psychiatry and Behavioral Science, University of Texas Medical School, PO Box 20708, Houston, TX 77025 **Drug treatment of depression: a classification system for agent selection.** Postgraduate Medicine. 67(5):153-156, 159, 161, 1980.

The use of drugs in the treatment of depression is discussed. A careful diagnosis is necessary in order to determine the type of depression (primary or secondary). In addition, the appropriate agent and dosage depends on the age of the patient, previous response to various medications, concurrent medical conditions, other medications being taken, and potential side-effects of the antidepressants. The dosage range, major indications, and side-effects of tricyclic antidepressants, monoamine oxidase inhibitors, lithium, neuroleptics, and benzodiazepines are described. 12 references.

10 DRUG TRIALS IN NEUROSES

004536 Aden, Gary C.; Thein, Stephen G., Jr. 3563 Fourth Avenue, San Diego, CA 92103 **Alprazolam compared to diazepam and placebo in the treatment of anxiety.** Journal of Clinical Psychiatry. 41(7):245-248, 1980.

Alprazolam was compared to diazepam and placebo in 235 outpatients suffering from manifest anxiety in a 28 day double-blind design. Alprazolam was more effective than placebo and essentially equivalent to diazepam in alleviating the symptoms of anxiety. However, alprazolam produced a markedly lower incidence of side-effects than either diazepam or placebo. Drowsiness was reported less than half as frequently by alprazolam patients than by diazepam patients. These results are achieved with an average daily dose of 1.5mg alprazolam compared to 18.6mg diazepam. 9 references. (Author abstract)

004537 Defayolle, M.; Bougeant, J. C. Centre de Recherches du Service de Sante des Armees (C.R.S.S.A.), 108, boulevard Pinel, F-69272 Lyon Cedex 1, France **/Study of a new molecule with anxiolytic effects (10 184 CERM)./** Etude des effets d'une nouvelle molecule a visee anxiolytique (10 184 CERM). Psychologie Medicale. 11(1):233-243, 1979.

A new molecule with anxiolytic effects (10 184 CERM) was studied in 16 volunteers divided into two homogenous groups. After a 3 day observation period without treatment, the patients received either 300mg of 10 184 CERM daily in three intakes, or a placebo for 4 days. The molecule was found to have an anxiolytic action without negative effect on vigilance. 8 references. (Journal abstract)

004538 Donlon, Patrick T.; Singer, Jack M. Dept. of Psychiatry, University of California/Davis, Sacramento, CA 95817 **Clobazam versus placebo for anxiety and tension in psychoneurotic outpatients. A multicenter collaborative study.** Journal of Clinical Pharmacology. 19(5-6):297-302, 1979.

Clobazam, a 1,5-benzodiazepam, was compared with placebo in 190 psychoneurotic outpatients with prominent symptoms of anxiety and tension of at least 2 weeks duration. Results showed that clobazam was an effective anxiolytic agent during the first week of treatment. Symptoms of psychic anxiety, autonomic symptoms, anxious mood, tension, and insomia were particularly responsive to treatment with clobazam. The incidence of side-effects was somewhat higher than expected, possibly due to the rapid escalation of dose from 40 to 80mg over the course of the week. 8 references.

004539 Evans, Larry; Best, Jeannette; Moore, George; Cox, John. Dept. of Psychiatry, Princess Alexandra Hospital, Brisbane, Queensland, 4102, Australia **Zimelidine -- a serotonin uptake blocker in the treatment of phobic anxiety.** Progress in Neuro-Psychopharmacology. 4(1):75-79, 1980.

An uncontrolled study of zimelidine, a new bicyclic antidepressant which causes relatively selective inhibition of serotonin uptake, and little effect on noradrenaline uptake in CNS neurons, is reported in five patients diagnosed as suffering from phobic anxiety. Results suggest that zimelidine has an antiphobic effect in some patients with phobic anxiety. The clinical impression gained is that three patients responded to treatment with zimelidine, and that side-effects were not severe, except in one patient who dropped out as a result of severe headaches related to zimelidine. It is concluded that a double-blind study comparing zimelidine and placebo in the treatment of phobic anxiety is justified. 12 references. (Author abstract modified)

004540 Gorski, Henryk; Kocur, Jozef; Sklodowski, Henryk. Instytut Higieny Psychicznej WAM, ul. Aleksandrowska 159, 91-229 Lodz, Poland /**Atypical central side-effects after low doses of propranolol in patients with anxiety neurosis.**/ Nietypowe osrodkowe objawy uboczne po niskich dawkach propranololu u chorych z nerwica lekowa. Psychiatria Polska. 13(6):601-605, 1979.

A detailed case history of two patients with anxiety neurosis who were treated with propranolol is presented. Both patients exhibited heightened anxiety states in the intermediate stages of the treatment. The treatment, which was continued to normal completion, was successful in both patients. It is noted that both patients had suffered brain concussions as children, which may have led to their heightened sensitivity to propranolol treatment. 16 references.

004541 Lowenkron, Theodor. Rua Figueiredo Magalhaes, 226/805, 22031 Rio de Janeiro, Brazil /**The utilization of psychotropic drugs in association with systematic psychotherapy.**/ A utilizacao de psicotropicos em associacao com psicoterapia sistematizada. Jornal Brasileiro de Psiquiatria. 29(1):27-31, 1980.

The utilization of psychotropic drugs in association with psychotherapy, particularly psychoanalysis, is discussed. Drugs used in the treatment of neurotic disorders are presented and include anxiolytic and antidepressive drugs. The basic treatment of neuroses in conjunction with incapacitating anxiety or severe depression drugs are also indicated. The advantages and disadvantages of the association between psychotherapy and drug treatment are given. It is concluded that only careful evaluation of each case will allow for the proper combination of drug and psychological therapy. 8 references. (Journal abstract modified)

004542 Moskowitz, Joel A. Calabasas Mental Health Services, 5734 Ostin Ave., Woodland Hills, CA 91367 **Lithium and lady luck: use of lithium carbonate in compulsive gambling.** New York State Journal of Medicine. 80(5):785-788, 1980.

Three case histories are described in which lithium carbonate was successfully used in patients who were compulsive gamblers. The patients exhibited and admitted to feelings of confidence, enthusiasm, fear, and guilt that drove them towards gambling. Lithium carbonate seemed to blunt this affective component with a concomitant salutory effect on their personal lives. 4 references. (Author abstract modified)

004543 Munford, Paul R. 750 Westwood Plaza, Los Angeles, CA 90024 **Haloperidol and contingency management in a case of anorexia nervosa.** Journal of Behavior Therapy and Experimental Psychiatry. 11(1):67-71, 1980.

The effects of haloperidol and contingency management on weight gain and hyperactivity were assessed in a 17-year-old hospitalized anorectic female. Following a baseline phase, the treatment consisted of six phases: 1) haloperidol and artane only, 2) haloperidol combined with reinforcement and feedback for weight gain, 3) haloperidol, placebo, artane, reinforcement and feedback for weight maintenance, 4) placebo, artane, reinforcement, and feedback for weight maintenance, 5) placebo discontinued, and 6) fading of reinforcement and feedback. The results do not permit conclusions to be drawn regarding the relationships between pharmacology and behavioral treatments of anorexia nervosa. However, findings demonstrate the potential of single subject experimental analysis in assessing pharmacotherapy combined with behavior therapy for anorectic patients. 10 references. (Author abstract modified)

004544 Rabavilas, Andrew D.; Boulougouris, John C.; Perissaki, Cleopatra; Stefanis, Costas. Dept. of Psychiatry, Athens University Medical School, Eginition Hospital, 74 Vas. Sophias Ave., Athens (611), Greece **The effect of peripheral beta-blockade on psychophysiologic responses in obsessional neurotics.** Comprehensive Psychiatry. 20(4):378-383, 1979.

To examine the effect of peripheral beta blockade on psychophysiologic responses in obsessional neurotics, 12 obsessive-compulsive patients were allocated randomly to two order groups of six patients each and were tested via a crossover design. One group had a psychophysiologic assessment before practolol administration. Four drug free days elapsed and then patients were placed on 300mcg of practolol, divided into two daily doses for 3 consecutive days, followed by a second identical assessment. The other group underwent the same procedure, but in the reverse order. Results show that a significant decrease in subjective anxiety, heartrate, and skin conductance amplitude occured after drug administration, but not during the drug free period. Results suggest that autonomic accompaniments of obsessive-compulsive symptomatology respond favorably to peripheral beta blockade, however, this was not shown to influence the whole clinical symptomatology. 13 references.

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

004545 Allain, H.; Van den Driessche, J.; Bentue-Ferrer, D.; Reymann, J. M.; Pape, D.; Madigand, M. Laboratoire de Pharmacologie, Faculte de Medecine, F-35043 Rennes, France **Plasmatic renin activity in patients treated with L-dopa and inhibitor of dopa decarboxylase (IDC).** Psychopharmacology. 61(2):197-202, 1979.

Plasmatic renin activity (PRA) was studied in patients receiving L-dopa, together with a decarboxylase inhibitor (IDC), at rest times and after periods of physical exertion. Untreated parkinsonian patients (n=12) showed PRA figures that were not significantly different from those of control Ss, while treated,

stabilized parkinsonian patients (n=14) showed increased PRA. A definite correlation between the increase in PRA and intensity of the dyskinesia is reported. Dosage is the only other factor differentiating the two groups of parkinsonian patients treated. Results are discussed in relation to arterial pressure in the various groups. 26 references. (Author abstract modified)

004546 Auriol, B.; Bardou, E.; Lambic, C. 18, Rue Notre Dame, F-31400 Toulouse, France **Control experiment in man on the sedative effect of disulfiram, an inhibitor of dopamine-beta-hydroxylase.** Biological Psychiatry. 15(4):623-625, 1980.

The sedative effect of disulfiram, an inhibitor of dopamine-beta-hydroxylase on 30 patients with psychomotor excitement was tested. Disulfiram proved to be superior to placebo in obtaining sedation of psychomotor excitement. The results suggest a higher efficiency with manic patients. Therefore, it is concluded that there are two kinds of psychomotor excitement; excitement due to nonadrenaline controlled by disulfiram and found in manic patients, and excitement due to dopamine controllable by dopamine blocking agents and found in schizophrenic patients. 15 references.

004547 Bendarzewska-Nawrocka, Barbara; Pietruszewska, Ewa; Stepien, Lucjan; Bidzinski, Jerzy; Bacia, Tadeusz. Klinika Neurochirurgii AM, Banacha 1a, 02-097 Warsaw, Poland **/Relationship between the levels of phenobarbital and diphenylhydantoin in patients with drug resistant epilepsy and therapeutic results and other clinical data./** Stosunek miedzy poziomem luminalu i dwufenylhydantoiny u chorych z lekooporna padaczka a wynikami leczenia i innymi danymi klinicznymi. Neurologia i Neurochirurgia Polska. 14/30(1):39-45, 1980.

A statistical analysis of the levels of phenobarbital (PH) and diphenylhydantoin (DPH) in a group of 100 patients with different types of epilepsy is reported. The mean values of PH and DPH were compared with the types of epilepsy, duration of the disease, additional treatment, EEG changes, and therapeutic results. The analysis indicated that the therapeutic range of the PH and DPH levels in this patient group was greater than those in other groups. No significant correlation was found between the levels of these drugs and the type of epilepsy, disease duration and EEG changes, with the exception of a positive correlation with PH level. Clonazepam, diazepam and mysodin raised the serum PH level in the serum, while only amizepine raised the DPH level. Higher levels of PH and DPH were found in patients with poor therapeutic results. 12 references. (Journal abstract modified)

004548 Bente, D.; Glatthaar, G.; Ulrich, G.; Lewinsky, M. Abt. f. Psychophysiologie der Freien Universitat, Nussbaumallee 26, D-1000 Berlin 19, Germany **/Quantitative EEG examinations on the vigilance stabilizing effect of nicergoline: results of a double-blind study with gerontopsychiatric patients./** Quantitative EEGUntersuchungen zur vigilanzfordernden Wirkung von Nicergolin: Ergebnisse eiher Doppelblindstudie bei gerontopsychiatrischen Patienten. Arzneimttel Forschung 29(11):1804-1808, 1979.

A randomized double-blind, crossover study was conducted on long-term gerontopsychiatric patients to compare the EEG effects of a 4 weeks' treatment with 10-methoxy-1,6-dimethyl-ergoline-8B-methanol-(5-bromonicotinate) (nicergoline, Sermion) with those of dihydroergotoxin-mesylate (DHETM) and a 4 weeks placebo period. The results of the power spectrum analysis with a consecutive factor analysis of the spectral data show that nicergoline and DHETM have a vigilance stabilizing effect which is characterized by a decrease in the relative power of slow delta-theta frequencies and an increase in the alpha power. As opposed to DHETM, for which this effect could not be proven, nicergoline produces a significant increase in the alpha power. As opposed to DHETM, for which this effect could not be proven, nicergoline produces a significant increase in power of the fast alpha frequencies as well as of the beta 1, beta 2, and beta 3 band. 13 references.

004549 Branconnier, Roland J.; Cole, Jonathan O.; Gardos, George. Geriatric Psychopharmacology Unit, Boston State Hospital, 591 Morton Street, Boston, MA 02124 **ACTH 4-10 in the amelioration of neuropsychological symptomatology associated with senile organic brain syndrome.** Psychopharmacology. 61(2):161-165, 1979.

Eighteen male and female volunteers over the age of 60 years who exhibited mild senile organic brain syndrome were administered ACTH 4-10 (Org 0I 63) or saline in a Latin square evaluation of ACTH 4-10. Subjects experienced a reduction in depression and confusion and an increase in vigor. This evidence of an increase in vigor was supported behaviorally by a delay in the onset of increased latency in reaction time. Data also indicate that retrieval from memory may be enhanced by this compound. The electroencephalogram evinced a shift to lower frequencies under ACTH 4-10, but this effect was primarily noted in the females who received drug followed by placebo. These effects suggest the need for further experimentation with ACTH 4-10. 24 references. (Author abstract modified)

004550 Briggs, R. S.; Castleden, C. M.; Kraft, C. A. Leicester General Hospital, Leicester LE5 4PW, England **Improved hypnotic treatment using chlormethiazole and temazepam.** British Medical Journal. No. 6214:601-604, 1980.

The hypnotic effects of a single 384mg oral dose of chlormethiazole were compared with those of 20mg temazepam in 10 old and 10 young healthy female volunteers (72.9 and 24.7 years old, respectively). Both drugs were effective hypnotics and had no detectable pharmacological action the next morning. Even 4 hours after administration, performance of a simple psychomotor test was not impaired and sway (measured by an ataxiameter) was not increased in either age group. Pharmacokinetic studies showed that chlormethiazole was rapidly absorbed, distributed, and eliminated in both groups, so that minimal plasma concentrations existed 11 hours after administration. Temazepam, however, was less quickly absorbed and distributed, especially in the young group, and substantial amounts remained in the plasma 11 hours after administration. No unwanted effects occurred after temazepam, but 17 of the 20 subjects suffered from nasal irritation after taking chlormethiazole. Thus, hangover effects may be avoided in elderly subjects after they have taken hypnotic drugs, and temazepam and chlormethiazole allow sleep to be interrupted safely. 23 references. (Author abstract)

004551 Brown, Gerald, L.; Hunt, Robert D.; Ebert, Michael H.; Bunney, William E., Jr.; Kopin, Irwin J. Rm 3N-204, NIH Clinical Center, 9000 Rockville Pike, Bethesda, Md 20205 **Plasma levels of d-amphetamine in hyperactive children.** Psychopharmacology. 62(2):133-140, 1979.

A pharmacokinetic study of a single oral dose of d-amphetamine in hyperactive children is presented. Sixteen children who scored less than 2 SD from norms on Factors I and IV of Conner's Teacher Rating Scale had a plasma d-amphetamine apparent elimination half-life of 6.8 plus or minus 0.5 h. Peak plasma level occured between 3 and 4 h. Six of the children had a reapeat study and there were no significant differences within subject in apparent elimination half-lives and attained peak blood levels. The variation in plasma levels was greater during absorption than during elimination. Both behavioral and motor activity responses as analyzed by differences between amphet-

amine and placebo days indicate significant responses between hours 1 through 4, however, these responses do not correlate with plasma amphetamine levels; they occur during the absorption phase. The decreased response to later similar plasma levels of d-amphetamine may be related to depletion of catecholamine stores, to replacement by a false neurotransmitter metabolite of amphetamine, or to alteration in receptor sensitivity. 87 references. (Author abstract modified)

004552 Bussone, G.; Boiardi, A.; Merati, B.; Crenna, P.; Picco, A. Centro Cefalee-Istituto Neurologico N. 11, I-20133 Milano, Italy **Chronic cluster headache: response to lithium treatment.** Journal of Neurology. 221(3):181-185, 1979.

The effects of lithium carbonate treatment on chronic cluster headache were investigated. Subjects were 20 patients who had been treated unsuccessfully for chronic cluster headache over the past 3 years. Blood levels of lithium were monitored. All patients showed improvement within a week of commencement of treatment. The mechanism of action is not clear. It is concluded that lithium is an effective therapeutic agent for chronic cluster headache patients. 15 references.

004553 Calne, Donald B.; Williams, Adrian; Eisler, Toomas; Teravainen, Heikki. Experimental Therapeutics Branch, NINCDS, NIH, Bethesda, MD **Current approaches to Parkinsonism.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1547-1553).

The role of dopamine (DA) in the control of motor function and in Parkinson's disease is discussed. The subdivision of DA receptors into different categories and the separation of monoamine oxidase isoenzymes A and B have permitted substantial advances in research in this area. The therapeutic effect of dopaminergic antiparkinson agents appears to depend on stimulation of a DA receptor independent of adenylate cyclase, while activation of the DA receptor coupled to this enzyme may have deleterious effects. Monoamine oxidase type-B appears to be involved in the degradation of brain DA, while the type-A enzyme is involved in norepinephrine degradation. These advances have permitted the development of more specific antiparkinson agents. The etiology of idiopathic Parkinsonism has not been clarified, but various features of the disorder appear to be associated with premature or accelerated aging of dopaminergic neurons. 40 references. (Author abstract modified)

004554 Campbell, Magda. Dept. of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Psychopharmacology.** In: Harrison, S., Therapeutic interventions. New York, Basic Books, 1979. 704 p. Vol. 3. (p. 376-409).

An overview of the current status of psychopharmacology in the treatment of moderately to severely disturbed children is presented. The history of psychopharmacology, the rationale that underlies psychopharmacology, the methodology of drug studies, indication for use of drug treatment, and technique are discussed. Neuroleptics, antidepressants, psychomotor stimulants, sedatives, hypnotics and anticonvulsants, anxiolytics, lithium, L-dopa, hallucinogens, megavitamins, and triiodthyronine are reviewed. The relationship of psychopharmacology to other modalities of treatment and what is known about outcomes or therapeutic results are discussed. 323 references.

004555 Casey, Daniel E.; Gerlach, Jes; Simmelsgaard, Hans. Dept. of Psychiatry, Veterans Administration Hospital, Portland, OR 97201 **Sulpiride in tardive dyskinesia.** Psychopharmacology. 66(1):73-77, 1979.

Sulpiride (400 to 2100mg/day), a selective type 2 dopamine receptor antagonist, was evaluated in a blind, placebo controlled trial in 11 patients with tardive dyskinesia. Sulpiride significantly reduced tardive dyskinesia without significantly affecting parkinsonism, although three patients had an increase in preexisting parkinsonian hypokinesia and tremor. During the placebo phase, the tardive dyskinesia and parkinsonian scores returned to the pretreatment values. There was no relationship between either tardive dyskinesia or parkinsonism and eyeblinking rates. These results are consistent with the hypothesis that more than one population of dopamine receptors are involved in controlling extrapyramidal function. Data indicate that sulpiride is an important tool for elucidating both the practical and heuristic aspects of subtypes of dopamine receptors and is a lead in the search for compounds that selectively affect dopaminergic mechanisms. 27 references. (Author abstract modified)

004556 Church, Michael W.; Johnson, Laverne C. Naval Health Researh Center, San Diego, CA 92152 **Mood and performance of poor sleepers during repeated use of flurazepam.** Psychopharmacology. 61(3):309-316, 1979.

The effects of flurazepam on the mood and performance of poor sleepers were studied over a 10 day drug period. Twelve poor sleepers, selected on the basis of subjective and objective criteria, were divided into two equal groups after a 7 day placebo baseline period. One group received 30mg flurazepam 15 minutes before bedtime for 10 consecutive nights while the other group continued to receive placebo in a double-blind paradigm. Three placebo followup nights were run on each S 2 to 3 weeks after the final drug night. Performance was tested in the morning, 30 to 45 minutes after arousal. Flurazepam significantly impaired performance on a 4 choice reaction time task and the Digit Symbol Substitution Test but not on a short-term memory test. Performance impairment on the DSST showed a drug tolerance effect across the 10 day drug period while performance impairment on the reaction time task showed no tolerance effect. Flurazepam had no significant effect on mood or feelings of sleepiness in the morning or at bedtime despite subjective ratings of a more restful and better sleep and improved sleep latencies. The placebo baseline mood and performance of the 12 poor sleepers were compared to the mood and performance of 12 good sleepers. Performance did not differe significantly between the two groups. Poor sleepers rated themselves as significantly more tense, confused, fatigued, and less vigorous than the good sleepers. 35 references. (Author abstract modified)

004557 Cohen, Ira L.; Campbell, Magda; Posner, Donn. Dept. of Psychiatry, New York University Medical Center, New York, NY **A study of haloperidol in young autistic children: a within-subjects design using objective ratings scales.** Psychopharmacology Bulletin. 16(3):63-65, 1980.

A within Ss study of haloperidol in young autistic children, which employed objective rating scales to assess drug effects, is described. Nine autistic children between the ages of 2.1 and 7.0 years participated in the double-blind, placebo controlled study, and were rated daily on a measure of the percent occurrence of predefined behaviors and on a scale designed to assess the extent the child would attend to the rater when asked to do so. Haloperidol was found to be effective in reducing high rates of stereotypy, and in increasing low rates of orienting to the rater. 4 references.

004558 Cole, J. O. Boston State Hospital, Boston, MA 02124 **Drug therapy of senile organic brain syndromes.** Psychiatric Journal of the University of Ottawa. 5(1):41-52, 1980.

Drug therapy in senile organic brain syndromes is reviewed. The concept of dementia is discussed. Memory impairment accompanied by impairment of abstractive thinking, impaired judgment, or personality change with or without deficiency in

impulse control are elements of the disorder. The great variety of pharmacologic agents currently available for the treatment of senile dementia is critically reviewed. They include the cerebral vasodilators (papaverine, dihydrogenated ergot alkaloids, hyperbaric oxygen), stimulants (analeptics, amphetamine-like drugs), and cholinergic agents. 107 references. (Author abstract modified)

004559 Conners, C. Keith; Taylor, Eric. Dept. of Psychiatry, Children Hospital National Medical Center, 111 Michigan Ave. NW, Washington, DC 20010 **Pemoline, methylphenidate, and placebo in children with minimal brain dysfunction.** Archives of General Psychiatry. 37(8):922-930, 1980.

An 8 week double-blind comparison between pemoline (Cylert), methylphenidate (Ritalin) hydrochloride, and placebo was carried out on 60 hyperactive children exhibiting minimal brain dysfunction. Measurements of home, school, achievement, cognitive function, and global clinical status were made at baseline, midtreatment, end of treatment, and posttreatment. Both drugs produced improvement in all areas except the achievement measures. One major difference between drugs was the apparently longer action of pemoline, since its effects at home and school tended to persist when the drug was withdrawn, whereas the patients receiving methylphenidate tended to regress to their baseline needs. 9 references. (Author abstract)

004560 Covanis, A.; Jeavons, P. M. 42 Westfield Road, Edgbaston, Birmingham B15 3QG, England **Once-daily sodium valproate in the treatment of epilepsy.** Developmental Medicine and Child Neurology. 22(2):202-204, 1980.

Evidence for the complete control of seizures in 35 epileptic patients is reported with the use of monotherapy with enteric coated sodium valproate. The drug was administered once daily, usually at night. The mean serum levels in seven patients were the same whether the drug was taken once or twice daily. The mean serum level was 65.4mg/1 on a mean daily dose of 19.5mg/kg. Drowsiness in the morning occurred in four patients, but only one had to return to twice daily administration. Compliance also improves with once daily administration. 4 references. (Author abstract)

004561 Cranford, Ronald E.; Leppik, Ilo E.; Patrick, Barbara; Anderson, Charles B.; Kostick, Barbara. Dept. of Neurology, Hennepin County Medical Center, 701 Park Ave. South, Minneapolis, MN 55415 **Intravenous phenytoin in acute treatment of seizures.** Neurology. 29(11):1474-1479, 1979.

Large doses of phenytoin were administered on 159 occasions to adult patients who had had more than three seizures or were in status epilepticus. Of the 139 patients treated, excellent responses were seen in 75 known epileptics with exacerbation of seizures, 6 cases of atypical alcohol withdrawal, and 17 miscellaneous conditions. Poor results were obtained in patients with anoxic or metabolic encephalopathy, stroke or other vascular diseases, brain tumors, or trauma. 25 references. (Author abstract modified)

004562 Crowley, Thomas J.; Jones, Richard H.; Hydinger-Macdonald, Marilyn J.; Lingle, James R.; Wagner, Janice E.; Egan, Donald J. Dept. of Psychiatry, University of Colorado Medical Center, Denver, CO 80262 **Every-other-day acetylmethadol disturbs circadian cycles of human motility.** Psychopharmacology. 62(2):151-155, 1979.

Two successive 24 h cycles of spontaneous motor activity were recorded from 12 patients receiving 1-alpha-actylmethadol (LAAM) every other day, and from five receiving methadone every day. LAAM patients were about 50% more active on days of drug administration than on nondrug days. There were no significant day to day differences in motility of methadone patients. LAAM administered every other day may significantly modify the human circadian rhythm of spontaneous motility. It is suggested that further research is needed before this treatment is widely adopted for treating heroin addicts. 18 references. (Author abstract modified)

004563 Danjoux, Jacques; Moron, Pierre Service Medico-Psychologique du C.H.U.R. de Toulouse-Rangueil, chemin du Vallon, F-31052 Toulouse, France /**Experimentation with viloxazine in child psychiatry.**/ Experimentation de la viloxazine en psychiatrie infantojuvenile. Psychologie Medicale. 11(1):191-197, 1979.

The effectiveness of viloxazine as an antidepressant was studied in 30 children and adolescents. It proved to be effective in depressive states in which inhibition, passivity, and anorexia predominated and for psychotic depressions and in neuroleptic-induced depressive states. Although the number of patients treated was too small to draw conclusions, viloxazine seemed to be beneficial in treating behavior and character disturbances. Tolerance was found to be good. Anxiety did not occur frequently and was predictable. Vascular side-effects were slight and transient and were most probably not due to the product. 47 references. (Journal abstract modified)

004564 Dasheiff, Richard M. Dept. of Neurology, Duke University Medical Center, Durham, NC 27701 **Benzodiazepine treatment for Lesch-Nyhan syndrome?** Developmental Medicine and Child Neurology. 22(1):101, 1980.

The use of benzodiazepine in alleviating the neurological and behavioral symptoms of the Lesch-Nyhan syndrome is discussed. Since hypoxanthine is markedly elevated in the cerebrospinal fluid of patients with this syndrome, it is hypothesized that pathological levels of purines in the brain may be antagonizing endogenous diazepam and providing the abnormal behavior. It is suggested that treatment with benzodiazepines would displace the purines at the receptor site and normalize the behavior.

004565 Dauverchain, J.; Choukroun, Pasturel; Pras, Rouy. no address /**Experimentation with Vincimax: 63 observations.**/ Experimentation sur Vincimax a propos de 63 observations. Revue de Geriatrie. 5(1):45-46, 1980.

The efficacy and tolerance of Vincimax in elderly persons was studied. The patients (26 men and 37 women over age 75) were administered the drug orally two times daily for 3 weeks, then three times daily for 3 months. Results show an improvement of all sensory disturbances and all psychological deficits. In the cases of behavior and mood disturbances, it was impossible to determine whether lack of improvement was due directly to the medication or was a result of the improvement of sensory and psychological disorders. It is concluded that Vincimax should be considered as one of the drugs used to improve sensory or psychological cerebral insufficiences.

004566 Dawling, Sheila; Crome, P.; Braithwaite, R. A.; Lewis, R. R. Poisons Unit, New Cross Hospital, Avonley Road, London, SE14 5ER, England **Nortriptyline therapy in elderly patients: dosage prediction after single dose pharmacokinetic study.** European Journal of Clinical Pharmacology. 18(2):147-150, 1980.

Sixteen depressed elderly hospitalized patients (mean age 81 years) received a single oral dose of nortriptyline prior to commencing treatment with this drug to determine appropriate dosage. Plasma nortriptyline measurements, after the single dose, were used to calculate the plasma drug clearance and to predict the daily dose required for each patient to achieve a

steady-state concentration within the suggested therapeutic range. Using these dosage regimens, the mean observed steady-state concentration showed significant correlation with the predicted values. All patients had steady-state concentrations within or very close to this suggested range. It is contended that use of the prediction test can prevent the development of toxic plasma concentrations and enhance the possibility of therapeutic success. These findings suggest that a safe starting dose of nortriptyline for the elderly is 30mg per day. 20 references. (Author abstract modified)

004567 de Montigny, C.; Chouinard, G.; Annable, L. Research Dept. Louis-H. Lafontaine Hospital, Montreal, Quebec, Canada H1N 3M5 **Ineffectiveness of deanol in tardive dyskinesia: a placebo controlled study.** Psychopharmacology. 65(3):219-223, 1979.

The effect of deanol in a group of patients whose tardive dyskinesia (TD) was aggravated by administration of a central anticholinergic drug was investigated. In a double-blind study, deanol was administered to chronic schizophrenic patients presenting severe and moderate TD. The drug failed to alleviate the dyskinetic movements. However, there was a tendency for a significant increase in the schizophrenic symptoms of the deanol treated group relative to the control group. The ineffectiveness of deanol in alleviating tardive dyskinesia is consistent with its inability to enhance brain acetylcholine synthesis. 70 references. (Author abstract modified)

004568 Di Donato, Romano. no address /**Combination of sulpiride and dimethyldiazepam in treatment of psychosomatic disturbances: a further experimental contribution.**/ Sulpiride e demetildiazepam in associazione nel trattamento di disturbi psicosomatici. Ulteriore contributo sperimentale. Medicina Psicosomatica. 24(1):53-60, 1979.

The utilization of sulpiride and dimethyldiazepam in the treatment of psychosomatic disturbances was studied. The sample consisted of 40 outpatients, 15 male and 25 female, suffering from psychosomatic disorders. Treatment consisted of daily administrations of three capsules containing a combination of 50mg of sulpiride and 5mg of demetildiazepam. The effects of the drug on the patients were expressed by three factors: results on the Foulds test, subject symptomatology, and symptomatology emerging from the doctor's interview. Results indicate that improvement was optimum in 10 cases, good in 15, mediocre in five, none in nine, and in one case the patient became worse. It is concluded that the use of these two drugs together is beneficial to patients suffering a variety of psychosomatic disorders. 4 references. (Journal abstract modified)

004569 Etevenon, P. Centre Hospitalier Sainte-Anne, rue Cabanis, F-75014 Paris, France **Effects of cannabis on human EEG.** In: Nahas, G., Marihuana: biological effects. Oxford, Pergamon, 1979. 777 p. (p. 659-663).

A review of research concerning the effects of delta9-tetrahydrocannabinol (THC) on the human EEG is presented. It is noted that a 10mg dosage produces quick shifts in vigilance levels with euphoric or dysphoric effects, arousal during the first 2 hours, then an increasing tendency to sleep in the last 6 hours. Low doses of THC induce specific psychophysiological and EEG effects which depend on the previous resting state and EEG baseline of the subjects. Through quantitative EEG changes is is possible to distinguish between body image distortions and visual hallucinations induced by THC. Additional studies of cannabinoids are needed in the field of quantitative EEG analysis correlated with pharmacokinetics, biochemical monitoring, psychophysiological rating scales, and behavioral studies. 12 references.

004570 Feely, Morgan; O'Callagan, M.; Duggan, B.; Callaghan, N. Callaghan: Cork Regional Hospital, Wilton, Cork, Ireland **Phenobarbitone in previously untreated epilepsy.** Journal of Neurology, Neurosurgery, and Psychiatry. 43(4):365-368, 1980.

Phenobarbitone was used to treat 13 new patients with epilepsy, and an attempt was made to determine the optimum dosage and plasma levels for the eight adult and five children. Full seizure control was achieved in 11 Ss and poor compliance was documented in one of the remaining two patients, in both of whom seizures were reduced by over 50%. Doses sufficient to give mean steady-state plasma levels of more than 43 micromol/l were associated with better seizure control than lower doses. No serious side-effects were observed. 13 references. (Author abstract modified)

004571 Fowler, L. K. Montedison Pharmaceuticals Ltd., Kingmaker House, Barnet, Hertfordshire, England **Post-marketing surveillance of Euhypnos (temazepam): a new hypnotic.** Journal of International Medical Research. 8(4):295-299, 1980.

Postmarketing surveillance was conducted of Euhypnos (temazepam), a new short acting benzodiazepine hypnotic. A total of 12,350 patients requiring a sleep inducer were treated for up to 3 months with doses of 10-30 mg at night. After 2 weeks, 80% of first reports (FRs) rated Euhypnos effective and at 3 months this had risen to 92% of 3062 second reports (SRs). Hangover was reported in 7% of FRs and 2% of SRs, but in general the drug was well tolerated with adverse reactions consisting mainly of morning nausea, headache, drowsiness and vivid dreaming. Eighty seven percent of FRs and 93% of SRs reported no hangover, adverse reaction, or any other type of event. 9 references. (Author abstract modified)

004572 Friis, M. L.; Johnsen, T.; Larsen, N. -E.; Hvidberg, E. F.; Pakkenberg, H. Dept. of Neurology, Rigshospitalet, 9 Blegdamsvej, DK-2100 Copenhagen, Denmark **Bromocriptine concentration in saliva and plasma after long-term treatment of patients with Parkinson's disease.** European Journal of Clinical Pharmacology. 18(2):171-174, 1980.

Salivary and plasma concentrations of bromocriptine (BCT), a dopamine agonist, were measured by gas chromatography in four patients with Parkinson's disease. All patients had been on monotherapy with BCT for years, and during the 3 weeks prior to the investigation they received constant but individually different dosage regimens. Paired samples of pure, parotid, serous saliva and of blood were collected hourly during one 8 hour dose interval. The concentrations of BCT in saliva were very low and there was a 10 fold range in the areas under the salivary and plasma concentration/time curves. It is concluded that in clinical practice, measurement of BCT in saliva is not suitable for exact estimation of the plasma concentration of BCT. Using the measured salivary pH and the plasma BCT concentration, calculations based on the Henderson/Hasselbalch equation showed that the assumption of about 99% plasma protein binding of BCT best fitted the observed concentrations of BCT in saliva. 11 references. (Author abstract)

004573 Gardos, George; Granacher, Robert P.; Cole, Jonathan O.; Sniffin, Celia. Institute for Research and Rehabilitation, 591 Morton Street, Boston, MA 02124 **The effects of papaverine in tardive dyskinesia.** Progress in Neuro-Psychopharmacology. 3(5/6):543-550, 1979.

The therapeutic efficacy of papaverine for tardive dyskinesia was tested in 23 psychogeriatric and 18 chronic schizophrenic patients. Papaverine was given in slow release capsules at 150mg BID for 1 week followed by 300mg BID for 5 weeks. A single-blind design was used with blind raters and a 6 week no drug control condition. Orofacial dyskinesia was significantly

reduced by papaverine in the psychogeriatric group during the first 6 weeks. Only a few patients showed at least 50% improvement of dyskinesia scores. Overall the drug effects were modest. Other findings include: 1) EEG showed increased percent time of alpha and reduced 2) Parkinsonian side effects;beta 1; 2) parkinsonian side-effects; 2) Parkinsonian side effects tended to confirm dopamine antagonism by papaverine; 3) no tolerance was seen after 6 weeks; and 4) elderly female patients and those with orofacial dyskinesia appeared to respond best to papaverine. 9 references. (Author abstract modified)

004574 Glotzner, F. L.; Miltner, F.; Kapp, G.; Pflughaupt, K. - W. Neurologische Universitatsklinik, DDR-8700 Wurzburg, Germany **Antiepileptic prophylaxis with carbamazepine in patients with severe head injuries.** Activitas Nervosa Superior. 21(4):244, 1979.

An ongoing study of the prophylactic effects of carbamazepine compared to placebo treatment in patients with substantial brain lesions is described. During the first 1.5 years of the study, 27 of 43 placebo patients had seizures compared with 14 of 38 carbamazepine treated patients. It was found that temporal lobe contusions are the lesions most likely followed by early or late seizures, and that carbamazepine prophylaxis is inefficacious in this type of lesion.

004575 Godwin-Austen, R. B.; Twomey, J. A.; Hanks, G.; Higgins, J. Dept. of Neurosurgery, Derbyshire Royal Infirmary, Derby, DE1 2QY, England **Oxpentifylline in Parkinson's disease.** Journal of Neurology, Neurosurgery, and Psychiatry. 43(4):360-364, 1980.

The effects of oxpentifylline were assessed in a double-blind trial in 11 patients with Parkinson's disease already under treatment. No significant improvement was noted. Eight patients developed involuntary movements or a worsening of movements if already present. The significance of these unexpected findings is discussed, and it is concluded that no change occurs in the therapeutic response to levodopa either subjectively or objectively when oxpentifylline is added to the treatment regimen. The results also raise the possibility of using the differential action of D1 and D2 dopamine receptor types to avoid some of the late hypersensitivity phenomena. 25 references. (Author abstract modified)

004576 Goldberg, Solomon C.; Casper, Regina C.; Eckert, Elke D. Virginia Medical College, Richmond, VA **Effects of cyproheptadine in anorexia nervosa.** Psychopharmacology Bulletin. 16(2):29-30, 1980.

The effects of cyproheptadine (Periactin) on weight gain and on various behaviors in anorexia nervosa were studied in a total of 105 rigorously diagnosed anorexia nervosa patients. Anorexia nervosa patients from three hospitals were randomly assigned to cyproheptadine or placebo and were followed in-house for 35 days. All patients received a ward milieu therapy in addition to study treatment. Random assignment to treatment followed a 7 day pretreatment period during which time the patients were assessed on a variety of measures for baseline purposes. Results are mixed, and provide some support for the drug's effectiveness in more severly ill patients. Strong effects of the drug on anorectic attitudes and behaviors were found, with only moderate or no effects on bodyweight. 10 references.

004577 Gottschalk, Louis A.; Cohn, Jay B. Dept. of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine, CA 92664 **Studies of cognitive function as influenced by administration of haloperidol or diazepam in detoxification of acute alcoholics.** Psychopharmacology Bulletin. 16(2):55-56, 1980.

The effects on cognitive functions of administration of haloperidol or diazepam in detoxification of acute alcoholics were investigated. Though clinical improvement of acute alcoholism followed these parenteral injections of haloperidol or diazepam, no significant consistent improvement occurred in these objective scores of cognitive impairment over a 4 hr period following drug administration. Neuropsychological test measures and the brain functions they assess were found to be variously influenced by alcohol intoxication. The development of neuropsychological test scores from speech samples is noted. 3 references.

004578 Gralewski, Zdzislaw; Pociecha-Lesniak, Maria. ul. Gliwicka 33, 44-2200 Rybnik, Poland **/Disorders in the calcium/phosphate balance in epileptic patients undergoing psychiatric treatment./** Zaburzenia gospodarki wapniowo-fosforanowej u chorych na padaczke leczonych w szpitalu psychiatrycznym. Psychiatria Polska. 13(6):549-554, 1979.

The effect of the calcium/phosphate balance in epileptic patients undergoing prolonged treatment in a psychiatric clinic was examined in 24 epileptic patients receiving anticonvulsant and neuroleptic drugs, 28 mentally ill patients receiving neuroleptics alone, and 25 normal Ss serving as controls. A statistically significant increase in the activity of basic phosphates was found in epileptic patients as compared with controls. Nonepileptic mentally ill patients showed a higher level of inorganic phosphates than controls and epileptic patients treated in the same hospital. The total calcium level in the blood serum showed no statistically significant differences. Results suggest that the increase in basic phosphatase activity is due to the presence of osteomalatic processes in epileptic patients. The higher phosphate level in the blood serum of nonepileptic mentally ill patients may be related to the complex influences of prolonged hospitalization and treatment, while the decreased phosphate level in epileptic patients and the supposed normalization may be attributed to the combined effects of antiepileptic drugs. It is also suggested that epileptic patients likely to stay in a psychiatric hospital for a prolonged period should receive prophylactic doses of vitamin D. 19 references. (Journal abstract modified)

004579 Hacke, W. Abteilung Neurologie, Klinikum der RWTH Aachen, Goethestrasse, D-5100 Aachen, Germany **/The pharmacological management of aggressive and autoaggressive behaviour in mentally retarded patients with melperone./** Die pharmakologische Beeinflussung aggressiven und autoaggressiven Verhaltens bei Geistigbehinderten mit Melperone. Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(1):20-24, 1980.

The results of 1 year of melperone treatment with 18 mentally retarded female patients with severe aggressive and autoaggressive behavior are reported. Six patients also suffered from various epileptic seizures. A significant reduction of the target behavior; as measured by the AFGB, was found. The activity of alkaline phosphatase showed a significant tendency towards normalization. EEG controls of Ss with epileptic seizures showed no increase of epileptic activity. No severe side-effects were noticed. 7 references. (Journal abstract modified)

004580 Hall, James H.; Marshall, Paul C. Dept. of Neurology, NRMC, Portsmouth, VA 23708 **Clonazepam therapy in reading epilepsy.** Neurology. 30(5):550-551, 1980.

In a 19-year-old man with reading induced epilepsy, generalized seizures were preceded by myoclonus of the jaw. Although reading epilepsy is usually refractory to anticonvulsant therapy, treatment with clonazepam resulted in complete control of the involuntary movements precipitated by reading. 10 references. (Author abstract modified)

004581 Hoes, M. J. A. J. M.; Colla, P.; Folgering, H. Dept. of Psychiatry, Radboudhospital, Theodoor Craanenlaan 4, NL-6500 HB Nijmegen, The Netherlands **Clomipramine treatment of hyperventilation syndrome.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(1):25-28, 1980.

Six patients suffering from a hyperventilation syndrome for 3.4 plus or minus 1.2 years were treated with clomipramine. Ss had a lowered PAco2 at rest and an abnormal CO2 response curve. During the entire period, they had received unsuccessful treatment with anxiolytics and had undergone behavior therapy for the last 1 to 2 years without success. Both treatments were discontinued and the patients were placed on clomipramine, 25mg t.i.d. for 9 months. Their anxiety and hyperventilation attacks diminished after 1 month of treatment, while fear of attacks and phobias subsided after 2 months. Eighteen months after clomipramine therapy had been initiated, they were feeling well without medication. The possible mode of action of clomipramine on the hyperventilation syndrome via central serotonergic mechanism is discussed. 17 references. (Journal abstract modified)

004582 Homan, Richard W.; Vasko, Michael R.; Blaw, Michael. Dept. of Neurology, University of Texas Health Science Center, Dallas, TX 75235 **Phenytoin plasma concentrations in paroxysmal kinesigenic choreoathetosis.** Neurology. 30(6):673-676, 1980.

The minimum effective plasma concentrations of phenytoin were determined in five patients with paroxysmal kinesigenic choreoathetosis (PKC). Symptoms of PKC were controlled in three adults at plasma phenytoin concnetrations well below the therapeutic range for phenytoin in epilepsy, but PKC symptoms in two children were controlled at about the same phenytoin concentration needed to control epileptic seizures. Results suggest an age dependent change in PKC and suggest the clinical course of PKC may reflect delayed maturation of extrapyramidal systems. 21 references. (Author abstract modified)

004583 Johannessen, Svein I.; Henriksen, Olaf. Statens Senter for Epilepsi, N-1301 Sandvika, Norway **Comparative steady state serum levels of valproic acid administered as two different formulations -- Depakene and Orfiril.** Acta Neurologica Scandinavica. 60(6):371-374, 1979.

Steady state serum levels of valproic acid produced in 15 epileptic patients before and after a 1 week treatment with a plain tablet (Deprakine) or an enteric coated tablet (Orfiril) were investigated. The latter drug produced in most patients a higher drug fasting blood level than the uncoated preparation (22%). The enteric coated tablets were also better tolerated. 8 references. (Author abstract modified)

004584 Johansson, Folke; von Knorring, Lars. von Knorring: Department of Psychiatry, University of Umea, S 901 85 Umea, Sweden **A double-blind controlled study of a serotonin uptake inhibitor (zimelidine) versus placebo in chronic pain patients.** Pain. 7(1):69-78, 1979.

The hypothesis was tested that a selective activation of the serotonergic pathways could be effective in relieving pain. Forty patients with pain syndromes of both organic and psychogenic origin of at least 6 months duration were included in a double-blind controlled study of a new selective serotonin uptake inhibitor, Zimelidine, versus placebo. Patients in the Zimelidine group experienced significantly more pain relief and tended to be able to reduce their need for analgesics more often than the patients in the placebo group. In the Zimelidine group, four patients were excluded due to nausea and intestinal troubles versus only one patient in the placebo group. However, among the patients who completed the trial, the side-effects were mild. Experimental findings support the hypothesis that the brain and spinal cord neurotransmitter, serotonin, play a crucial role in nociception. 18 references. (Author abstract modified)

004585 Johnstone, Eve C.; Owens, D. G. Cunningham; Frith, C. D.; McPherson, Klim; Dowie, C.; Riley, G.; Gold, Aviva Divison of Psychiatry, MRC Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, England **Neurotic illness and its response to anxiolytic and antidepressant treatment.** Psychological Medicine. 10(2):321-328, 1980

Neurotic outpatients (n=240), allocated to no diagnostic category, were rated in terms of observer and self-ratings of both depression and anxiety at weekly intervals during a 4 week trial of amitriptyline, diazepam, amitriptyline and diazepam, or placebo. The sample could not be divided into anxious and depressed groups on the basis of the clinical picture. The outcomes tended to be good irrespective of medication, but the significant drug effects found were due to amitriptyline and concerned measures of anxiety as well as depression. It is concluded that a distinction between anxiety and depression in neurotic outpatients is of no practical value with regard to psychopharmacological treatment. 30 references. (Author abstract)

004586 Jost, F. Psychiatrische Klinik Beverin, Cazis, Graubunden, Switzerland /**The treatment and resocialization of sexual delinquents with antiandrogens and psychotherapy.**/ Zur Behandlung und Resozialisierung von Sexualdelinquenten mit Antiandrogenen und Psychotherapie. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie. 124(2):243-253, 1979.

Forty sexual offenders were treated with antiandrogens and both psychotherapy and sociotherapy for a period of 2 to 6 years. Topics included the pathogenesis of sexual perversion, treatment choice, therapeutic methodology, long-term therapy, provisional release problems, ambulatory treatment and prognosis. For 27 Ss, treatment terminated after 2 to 6 years. To date 70% of this group have not relapsed, while seven relapsed, all within the first year. The therapeutic results of the combined treatments are considered very good. 14 references. (Journal abstract modified)

004587 Kangas, Lauri; Kanto, J.; Lehtinen, V.; Salminen, J. M. Sci., Dept. of Pharmacology, Kiinamyllynkatu 10, SF-20520 Turku 52, Finland **Long-term nitrazepam treatment in psychiatric out-patients with insomnia.** Psychopharmacology. 63(1):63-66, 1979.

Psychiatric patients (N=26) were treated chronically (from 1 week to 12 years) with nitrazepam, because of insomnia. The patients gave their subjective estimations of the effects and side-effects of nitrazepam. The pharmacokinetics of nitrazepam were compared among psychiatric patients and healthy volunteers. The steady state concentrations and the half-life of nitrazepam in the psychiatric patients were comparable to those of the healthy volunteers. The subjective hypnotic effect of nitrazepam was mostly good or satisfactory and remained unchanged during long-term treatment. Nitrazepam does not seem to cause enzyme induction with lowered plasma levels and may therefore be of special value in the treatment of chronic insomnia. 19 references. (Author abstract modified)

004588 Kaye, Philip L. 32-06 29th St., Long Island City, NY 11106 **Fatigue: pervasive problem.** New York State Journal of Medicine. 80(8):1225-1229, 1980.

A common variety of fatigue, the pathogenesis and abnormal physiology of which may be attributed to an underlying chronic overactivity of the vagal parasympathetic system, is discussed. This overactivity can be demonstrated by changes in carbohydrate metabolism and in insulin production. The syndrome is

specific and frequent and the institution of treatment with atropine is indicated and is usually successful. The syndrome is best conceived as a physiologic reaction to stress. The fatigue syndrome is clearly diurnal with a cyclic rhythm, present on arising, then relieved, recurring in the afternoon, then relieved in the evening. The fatigue syndrome is not usually recognized as a syndrome, but is responsible for all or an important part of many disabling symptoms. A commentary by Burton M. angrist is included. 19 references. (Author abstract modified)

004589 Klein, Donald F. New York State Psychiatric Institute, New York, NY **Behavior therapy, supportive therapy, and imipramine in different classes of phobics.** Psychopharmacology Bulletin. 16(2):62-64, 1980.

The clinical efficacy of behavior therapy, supportive therapy, and imipramine in different classes of phobic patients is reviewed. The development of the manifest phobia is conceptualized as a three stage process: spontaneous panic attacks causing anticipatory anxiety which in turn causes avoidant behavior. Results indicate that imipramine is practically 100% effective in blocking panic attacks. It is contended that any technique that is persuasively effective can be expected to be helpful in the treatment of phobia. The idea that there are specific interventions, based on learning theory or dynamic theory, seems unsupported. For patients with spontaneous panic attacks, the use of antidepressants is often essential for progress. For patients dominated by pure anticipatory anxiety, antidepressants are ineffective. 4 references.

004590 Kurata, Koichi. Department of Neurology and Psychiatry, School of Medicine, Kanazawa University, Kanazawa, Japan **Studies on the serum levels of antiepileptic drugs -- with particular reference to diphenylhydantoin, phenobarbital and carbamazepine.** Psychiatria et Neurologia Japonica. 81(8):509-522, 1979.

The blood serum level of diphenylhydantoin (DPH), phenobarbital (PB) and carbamazepine (CBz) in 112 epileptic patients and its clinical significance were investigated. Gas chromatography with flash methylation technique was used, and quantitative determination of PB was also attempted. Relationships between dosage and blood serum level differed from one drug to another. DPH level rose abruptly at the dose of 4 to 6mg/kg/per day; PB level had correlations with dosage, $Y=0.6x \quad 4.8$ ($r=0.632$); CBZ presented $Y=0.2x \quad 2.6$ ($r=0.360$). Combined barbiturates resulted in higher serum level than PB alone with 23% showing 40mcg/ml which was in the border line of toxic dose. No circadian change in serum level was observed with administration of any of the three drugs three times a day. Chronological study of four cases suggested 12 to 14mcg/ml as a minimum effective DPH level for most cases from clinical point of view. 55 references.

004591 Kyriakides, Mary; Silverstone, Trevor; Jeffcoate, William; Laurance, Bernard. Academic Unit of Human Psychopharmacology, Medical College of St. Bartholomew's Hospital, London EC1A 7BE, England **Effect of naloxone on hyperphagia in Prader-Willi syndrome.** Lancet. No. 8173:876-877, 1980.

The effects of naloxone on hyperphagia in three patients with Prader-Willi syndrome were examined in a double-blind experiment. The results indicated that naloxone, especially at the higher doses, reduced food intake in the two male patients whose baseline food intake was abnormally high. It had no effect on the more modest intake of the female patient. All three patients complained of drowsiness after they had naloxone, which could possibly account for the lowered food intake. 7 references.

004592 Ladd, Marcia; Johnson, Dale T. Johnson: Texas Tech School of Medicine at El Paso **Behavioral effects of stimulant drugs in hyperkinetic children.** JSAS/Catalog of Selected Documents in Psychology (APA). 9(August):52-53,1979. MS. 1874, 38 p. paper: $6; fiche: $2.

An attempt to construct a composite interpretation of the heterogeneous nature of hyperkinesis that explains, at least partially, the diverse findings reported in the literature is presented. Four general areas are presented: 1) a discussion of current research data on the behavioral effects of amphetamine and methylphenidate on different types of hyperkinetic children, 2) an examination of existing findings concerning the long-term and short-term effects of these stimulants on a wide variety of behavioral measures, 3) a critical examination of the differential behavioral effects of amphetamine and methylphenidate, and 4) an attempt to integrate all of these findings into a comprehensive and clinically useful explanation of the behavioral effects of using stimulant medications to treat hyperkinesis. (Author abstract modified)

004593 Lake, C. R.; Mikkelsen, E. J.; Rapoport, J. L.; Zavadil, A. P., III; Kopin, I. J. Rapoport: NIMH, Unit on Childhood Mental Illness, Bldg. 10, Room 3N-204, Bethesda, MD 20205 **Effect of imipramine on norepinephrine and blood pressure in enuretic boys.** 6(5):647-653, 1979. Clinical Pharmacology and Therapeutics.

The effects of imipramine, desmethylimipramine, and methscopolamine on blood pressure (BP) and plasma norepinephrine (NE) were measured in enuretic boys in a double-blind, placebo controlled study. Measurements were obtained after 13 days on medication (75mg at bedtime). The tricyclic drugs induced a rise in diastolic BP and an increase in plasma NE, but there was no significant relationship between the increments in NE and BP. The plasma concentration of drug correlated with the drug induced rise in BP. The hypertensive effect of tricyclic drugs in children contrasts with the systolic hypotension usually seen in adult patients, possibly due to different cardiovascular compensatory reflexes or different sensitivities to the stimulant effects of the drug. 21 references. (Author abstract modified)

004594 Langwinski, Romuald. Instytut Patologii Klinicznej, Zaklad Farmakodynamiki AM, ul. Staszica 4, 20-081 Lublin, Poland **/Psychopharmacology and endorphins./** Psychofarmakologia a endorfiny. Psychiatria Polska. 13(6):533-542, 1979.

The structure and functioning of endorphins and their effect on mental illness are discussed. It is hypothesized that hyperfunctioning of endorphins is a contributing factor to schizophrenia, whereas hypofunctioning plays a role in emotional disturbances of a depressive nature. The effect of endorphins in neurotransmitors is examined, and the apparent inconsistencies in the results are explained in terms of multiple types of opiate receptors. The opiate receptors can respond so as to make the mediation appear to be an agonist or antagonist, depending upon which receptor is activated. This problem is further compounded by the existence of endogenic agents. Clinical studies are recommended to test these theories by studing the etiology of schizophrenia in relation to the various agonists and antagonists of opiate receptors. 40 references.

004595 Lindblom, Ulf; Tegner, Richard. Dept. of Neurology, Huddinge University Hospital, S-141 86 Huddinge, Sweden **Are the endorphins active in clinical pain states? Narcotic antagonism in chronic pain patients.** Pain. 7(1):65-68, 1979.

Naloxone was given, alternate with saline, in a double-blind study to 10 patients with chronic neuralgia or low back pain to test the possibility of endorphin release in clinical pain states. Results indicate that there was no significant alteration of the

levels of spontaneous pain or heat pain thresholds. The results suggest that the endorphin system does not offer protection of any importance in chronic pain. One possible explanation is that depletion of endorphins is a basis for the development of sustained pain, which is compatible with the observation of low CSF levels in some patients. Another possibility is that the endorphin system is not activated by clinical pain. 17 references.

004596 Linnoila, M.; Erwin, C. W.; Logue, P. E. Box 3870, Duke University Medical Center, Durham, NC 27710 **Efficacy and side effects of flurazepam and a combination of amobarbital and secobarbital in insomniac patients.** Journal of Clinical Pharmacology. 20(2-3):117-123, 1980.

Effects of two common hypnotics, flurazepam and a combination of amobarbital and secobarbital, on sleep, performance, and mood in severely insomniac patients, free of somatic and psychiatric illnesses, were investigated. The efficacy of the hypnotics was rated using a postsleep questionnaire every morning. The results indicate that flurazepam, 30mg, was not more effective in inducing sleep than placebo. Barbiturates (100mg amobarbital plus 100mg secobarbital) were more effective in inducing and maintaining plus 100mg secobarbital) were more effective in inducing and maintaining sleep than flurazepam or placebo. Contrary to work conducted in the sleep laboratory the barbiturate hypnotics were still effective on the fourteenth night. Insomniacs performed poorly on psychomotor tests, but as group they did not show statistically significant psychomotor impairment after the use of the hypnotics. 20 references. (Author abstract modified)

004597 Lockman, Lawrence A.; Kriel, Robert; Zaske, Darwin; Thompson, Theodore; Virnig, Norman. Division of Pediatric Neurology, University of Minnesota Medical School, Box 486, 420 Delaware St. SE, Minneapolis, MN 55455 **Phenobarbital dosage for control of neonatal seizures.** Neurology. 29(11):1445-1449, 1979.

The dose of phenobarbital required for seizure control was studied in relation to weight, gestational age, and blood level in 39 neonates. The blood level of phenobarbital was proportional to the dose per kg and was not related to weight or gestational age. Seizures remitted only when blood phenobarbital concentrations were greater than 16.9mcg per ml. Therapeutic levels could be achieved by intravenous or intramsucular administration of 16 to 23mg/kg phenobarbital. 8 references. (Author abstract modified)

004598 Loosen, Peter T.; Prange, Arthur J., Jr. Dept. of Psychiatry, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Thyrotropin releasing hormone (TRH): a useful tool for psychoneuroendocrine investigation.** Psychoneuroendocrinology. 5(1):63-80, 1980.

Behavioral and endocrine data were assessed following injection of the hypothalamic tripeptide TRH in 23 normal controls and 17 schizophrenic, 33 alcoholic, and 17 depressive patients. After TRH there was a brief and partial salutary behavioral change in all groups. A blunted thyroid stimulating hormone (TSH) response after TRH was seen in some depressed and some alcoholic patients, but not in schizophrenics. In depression, but not in alcoholism, the blunting was accounted for by increased levels of serum cortisol. While the relationship between ambient levels of serum cortisol and the TSH response was negative in normals and depressives, it was positive in schizophrenics. The data suggest that both the behavioral and endocrine effects of TRH render it useful for psychoneuroendocrine investigation. 69 references. (Author abstract modified)

004599 Luoma, Pauli V.; Myllyla, Vilho V.; Sotaniemi, Eero A.; Lehtinen, Inkeri A.; Hokkanen, Eero J. Clinical Research Unit, Dept. of Internal Medicine, University of Oula, SF-90220 Oulu 22, Finland **Plasma high-density lipoprotein cholesterol in epileptics treated with various anticonvulsants.** European Neurology. 19(1):67-72, 1980.

Plasma high density lipoprotein (HDL) cholesterol in 97 epileptics on long-term anticonvulsant therapy was investigated. Therapy with phenytoin alone or in combination with carbamazepine or phenobarbital was associated with elevated plasma HDL cholesterol levels as compared with controls. HDL cholesterol in patients treated with carbamazepine did not diverge from control values. Patients treated with phenytoin and phenobarbital in combination showed higher HDL cholesterol levels than those treated with phenytoin alone. There was an inverse correlation between the HDL cholesterol and serum triglyceride levels. The results demonstrate that high plasma HDL cholesterol might be associated with therapy involving some anticonvulsants known to be potent enzyme inducers. This suggests that the elevation of HDL cholesterol during therapy is probably related to the drug caused enzyme induction phenomenon. 20 references. (Author abstract)

004600 Marsh, Gail R.; Linnoila, Markku. Dept. of Psychiatry, Duke University Medical Center, Durham, NC 27710 **The effects of deanol on cognitive performance and electrophysiology in elderly humans.** Psychopharmacology. 66(1):99-104, 1979.

The effects of deanol on cognitive performance and electrophysiology of 11 elderly human Ss were investigated. Deanol (900mg/day for 21 days) had no effect on learning a list of words when tested at weekly intervals. Tests of simple and complex reaction time and a test of continous serial decoding of digits showed no enhancement with the drug. Several components of evoked potentials recorded from several scalp sites did show enhanced amplitude under drug treatment. These changes were not accompanied by changes in the EEG spectrum as are seen with some other psychoactive drugs. Deanol seems to be an ineffective treatment for the normal slowing of cognitive function seen in the normal elderly or those elderly with only a minimal cognitive decline and free of symptoms of demential. Contrary to earlier reports, elderly persons were found to be able to benefit from warning signals in a complex reaction time task. 40 references. (Author abstract modified)

004601 Mathieu, J.; Ginglinger, M.; Ullmann, P. Service de Readaptation Fonctionelle, Centre Hospitalier, Vichy, France / **Experimentation with piracetam (Nootropyl) in geriatrics in a functional rehabilitation service./** Experimentation du piracetam en geriatrie dans un service de readaptation fonctionnelle. Revue de Geriatrie. 4(4):189-191, 1979.

The telencephalic effects of piracetam were tested on 146 elderly patients in a functional rehabilitation service. Piracetam is a product which belongs to the class of nootropic drugs, is not metabolized, is not toxic. Neuropharmacological effects of the drug are described. The great diversity of the patients did not make it possible to establish a double-blind series. It is concluded that piracetam gives favorable results in clinical treatment of very old patients with serious medical history. Its tolerance is excellent. The use of the drug is fully justified. 16 references.

004602 Mattes, Jeffrey. Child Development Clinic, Long Island Jewish-Hillside Medical Center, New Hyde Park, NY **A pilot trial of amantadine in hyperactive children.** Psychopharmacology Bulletin. 16(3):67-69, 1980.

An open clinical trial of amantadine, a dopamine agonist thought to release stored dopamine, in nine hyperactive children is described. Amantadine was administered for 1 month at the dosage recommended for prophylaxis of Type A influenza, namely 200mg/day. Children were taken off stimulants during

and for 1 week prior to or following amantadine administration. Overall, only slight suggestive evidence that amantadine might be helpful in hyperactive children was found. A trial with higher dosage seems indicated. Since the margin of safety with amantadine is large, a dose might be found which would reduce hyperactive symptomatology significantly with only minimal side-effects. 12 references.

004603 McEntee, William J.; Mair, Robert G. Neurology Service, V.A. Medical Center, Providence, RI 02908 **Memory enhancement in Korsakoff's psychosis by clonidine: further evidence for a noradrenergic deficit.** Annals of Neurology. 7(5):466-470, 1980.

Three drugs, d-amphetamine, clonidine, and methysergide, which presumably enhance central noradrenergic activity by different pharmacological mechanisms, were administered to eight patients with the Korsakoff syndrome in a 2 week subacute, double-blind, counterbalance experiment to study the effects of these agents on memory function as measured by a neuropsychological test battery. Of the drugs tested, only clonidine, a putative alphanoradrenergic agonist, was associated with significant improvement in memory. The data are consistent with the hypothesis that damage to ascending norepinephrine containing neurons in the brainstem and diencephalon may be the basis for amnesia in Korsakoff's psychosis. 39 references. (Author abstract)

004604 Molnar, G. Clinic of Psychiatry, Semmelweis Medical University, Budapest, Hungary **Blood levels of antiepileptics in children.** Agressologie. 20(D):259-264, 1979.

Blood levels of diphenylhydantoin (DPH) and phenobarbital (PHB) and frequency of seizures were studied in a group of 42 epileptic children, aged 1 to 14, with relatively high seizure frequency. Even with a seemingly rational drug intake, there were many epileptic children with subtherapeutic DPH or PHB levels. In spite of only moderate correlations between drug level and seizure frequency, there is an evident need to maintain antiepileptics at a preventative, therapeutic level. At higher antiepileptic levels, considered toxic, children show a better tolerance than adults. A number of epileptic children need long-term comprehensive observation because of their drug unresponsiveness or intolerance. These patients are advised to submit to detailed clinical/pharmacological investigation including systematic drug monitoring, loading studies to clarify metabolic abnormalities, distribution in body systems, and drug interactions. 9 references. (Author abstract modified)

004605 Myrsten, Anna-Lisa; Rydberg, Ulf; Idestrom, Carl-Magnus; Lamble, Robert. Dept. of Psychiatry, University College, Dublin, Ireland **Alcohol intoxication and hangover: modification of hangover by chlormethiazole.** Psychopharmacology. 69(2):117-125, 1980.

Alcohol intoxication and hangover and the modification of hangover by chlormethiazole were studied in 12 healthy male Ss who participated in three 18 h experimental sessions. In one of the alcohol sessions, Ss received chlormethiazole, 1g at bedtime and 0.5g early the following morning; in the other alcohol session, Ss received placebo tablets. During intoxication (produced by 1.43g alcohol/kg), heartrate and lactate/pyruvate ratio were significantly increased and performance efficiency was significantly deteriorated in comparison with the control condition. During hangover, heartrate, blood pressure, and lactate/pyruvate ratio were significantly elevated, and cognitive performance was still affected, in some tests to a significant degree. During this stage, there was a great variation between Ss as regards subjective hangover. Chlormethiazole was found to lower blood pressure and adrenaline output and furthermore, to relieve unpleasant physical symptoms, but did not affect fatigue and drowsiness. The cognitive test results were only slightly influenced by this agent, while psychomotor performance was significantly impaired. Ss with severe subjective hangover seemed to benefit more from the chlormethiazole treatment than Ss with a mild hangover. 30 references. (Author abstract modified)

004606 no author. no address **Marijuana agent fails to fatten anorexics.** Medical World News. 21(14):17, 21, 1980.

The effect of marihuana on the appetite of anorexia nervosa patients was studied by doctors at the National Institute of Mental Health. The most psychoactive ingredient in marihuana, tetrahydrocannabinol (THC), did not seem to make the the anorexics hungry. The 11 severely anorexic patients who participated in the 4 week double-blind crossover study gained no more weight when taking THC than they did using diazepam, which served as a psychoactive placebo. Three of the 11 had severe paranoid reactions and complained of loss of control during the THC phase of the trial. However, some success with the total parenteral nutrition approach has been reported. Weight gain, improved nutrition, and marked improvement in behavior resulted in the adolescent Ss.

004607 Nurowska, Krystyna. Instytut Psychoneurologiczny, A1. Sobieskiego 1/9, 02-957 Warsaw, Poland **/A clinical evaluation of sulpiride./** Ocena kliniczna sulpirydu. Psychiatria Polska. 14(1):37-42, 1980.

A study evaluating the efficacy of sulpiride in the treatment of schizophrenia, endogenous depression, and hypochondriacal or hallucinatory syndromes of various etiology in 60 patients aged 22 to 77 years is presented. The drug was tested in a controlled open study for over 40 days. Results indicate that 33% of the patients were significantly improved, while in 70% beneficial affects of the drug were manifest. It was found that sulpiride is a quick acting drug and its action is beneficial in cases of lowered mood and in alleviating axial and productive schizophrenic symptoms. It was also found that side-effects are similar to those typical of neuroleptics, but take milder form. 12 references. (Journal abstract modified)

004608 O'Hare, J.; O'Driscoll, D.; Duggan, B.; Callaghan, N. Departments of Neurology and Biochemistry, St. Finbarr's Hospital, Cork, Ireland **Increase in seizure frequency following folic acid.** Irish Medical Journal. 72(6):241-242, 1979.

A case history is reported of a 27-year-old epileptic male with megaloblastic anemia who developed an increase in seizure frequency with a reduction in carbamazepine and phenobarbitone levels following treatment with folic acid. Seizure frequency was reduced following increases in dosage of carbamazepine to 1,800mg/day. The phenobarbitone dosage was maintained at 270mg/day. A reduction in seizure frequency following increased anticonvulsant dosage also resulted in a full response of the patient's anemia to folic acid at a dosage of 5mg daily. It is suggested that an increase in seizure frequency was due to the reintroduction of the microsomal enzyme system when phenobarbitone and carbamazepine levels fell following restoration of folate. Administration of folate supplements under hospital supervision, preferably with anticonvulsant blood level monitoring, is recommended. 6 references.

004609 Oshtory, Meherji A.; Vijayan, Nazhiyath. Vijayan: EEG Laboratory, University of California, Davis Medical Center, 2315 Stockton Blvd., Sacramento, CA 95817 **Clonazepam treatment of insomnia due to sleep myoclonus.** Archives of Neurology. 37(2):119-120, 1980.

Two cases of noctunal myoclonus are reported which responded well to small doses of clonazepam. Treatment with

1mg of clonazepam before retiring specifically controlled the myoclonus and allowed normal sleep patterns. In one patient, use of clonazepam is reported to have continued for one and a half years without difficulty. The other patient, however, experienced depression and discontinued drug therapy at which time the myoclonus returned. Findings are discussed in terms of the possible action of clonazepam. 5 references. (Author abstract modified)

004610 Petova, J.; Vinsova, N.; Benesova, O. Karlovo nam. 32, 120 00 Prague 2, Czechoslovakia **/Psychomotor development of high-risk newborn babies during early and long-term treatment with pyritinol./** Psychomotoricky vyvoj vysoce ohrozenych novorozencu pri vcasne a dlouhodobe aplikaci pyritinolu. Ceskoslovenska Neurologie a Neurochirurgie. 42/75(6):402-412, 1979.

The effect of pyritinol on the psychomotor development of newborn babies suffering from severe abnormalities was studied. A group of 128 high-risk infants, treated after delivery in an intensive care unit because of severe pathological symptoms caused by a high degree of prenatal and intranatal stress (protracted intrauterine malnutrition, hypoxia, immaturity), was studied by a team consisting of a child neurologist, a pediatrician, and a psychologist. Sixty six of these infants were given pyritinol from the third day after birth up to ages 4 to 12 months. Ath ages 1 to 7 years, the incidence of neurological disorders in the group treated with pyritinol was found to be 12%, in the control group 53%. The incidence of severe disorders such as DMO, epilepsy, and feeblemindedness was 7.5%, as compared to 38.7% in the control group. It is concluded that timely and long-term treatment with pyritinol is a suitable supplement for intensive neonatal care of high-risk infants for the prevention of possible damage to the central nervous system resulting from perinatal stress. 22 references. (Journal abstract modified)

004611 Porter, Roger J.; Penry, J. Kiffin; Lacy, Joseph R.; Newmark, Michael E.; Kupferberg, Harvey J. Epilepsy Branch, Federal Building, Room 114, National Institutes of Health, Bethesda, MD 20205 **Plasma concentrations of phensuximide, methsuximide, and their metabolites in relation to clinical efficacy.** Neurology. 29(11):1509-1513, 1979.

The clinical efficacy of phensuximide and methsuximide was studied in relation to plasma concentrations of these compounds and their desmethylmetabolites in five patients with intractable seizures. Phensuximide had a mean half-life of 7.8 hours and accumulated to an average fasting level of 5.7mcg/ml. Desmethylphensuximide averaged only 1.7mcg/ml, with a similar half-life. Methsuximide had a half-life of only 1.4 hours, but its desmethyl metabolite had a mean helf-life of 38 hours and accumulated to levels greater than 40mcg/ml. Phensuximide had no therapeutic effect in these patients, but two patients had an excellent response to methsuximide. Results indicate that the relatively weak antiepileptic effects of phensuximide are due to its failure to accumulate to adequate levels. 16 references. (Author abstract modified)

004612 Rapoport, J.; Elkins, R.; Mikkelsen, E. Unit on Childhod Mental Illness, Biological Psychiatry Branch, NIMH, Bethesda, MD **Clinical controlled trial of chlorimipramine in adolescents with obsessive-compulsive disorder.** Psychopharmacology Bulletin. 16(3):61-63, 1980.

A clinical controlled trial of chlorimipramine in nine adolescents with obsessive-compulsive disorders is described. The 16 week drug trial consisted of a 1 week baseline period followed by 3 to 5 weeks consecutive periods of treatment with either placebo, desmethylimipramine, or chlorimipramine. The children were given supportive psychotherapy and their parents were seen weekly for counseling. Results of this pilot trial indicate both the complexity of rating obsessive-compulsive behavior, at least in this age group, as well as the apparent lack of effect of chlorimipramine on the obsessional symptoms. Despite short-term improvement attributed to general support and removal from home, followup from 6 months to 2 years on this sample indicates that three of the eight children had had continued hospitalization following the study and two others have had periodic incapacitation from their disorder. 6 references.

004613 Rapoport, Judith L.; Buchsbaum, Monte S.; Weingartner, Herbert; Zahn, Theodore P.; Ludlow, Christine; Mikkelsen, Edwin J. Bldg. 10, Room 3N204, NIMH, Bethesda, MD 20205 **Dextroamphetamine: its cognitive and behavioral effects in normal and hyperactive boys and normal men.** Archives of General Psychiatry. 37(8):933-943, 1980.

The effects of a single oral dose of dextroamphetamine sulfate on motor activity, vigilance, learning, and mood were compared for normal and hyperactive prepubertal boys and normal college aged men using a double-blind crossover design. Both groups of boys and men showed decreased motor activity, increased vigilance, and improvement on a learning task after taking the stimulant drug. The men reported euphoria, while the boys reported only feeling tired or different after taking the stimulant. It is not clear whether this difference in effect on mood between adults and children is due to differing experience with drugs, ability to report affect, or a true pharmacologic age related effect. While there were some quantitative differences in drug effects on motor activity and vigilance between groups, stimulants appear to act similarly on normal and hyperactive children and adults. 55 references. (Author abstract)

004614 Rowan, A. J.; Binnie, C. D.; de Beer-Pawlikowski, N. K. B.; Goedhart, D. M.; Gutter, T.; van der Geest, P.; Meinardi, H.; Meijer, J. W. A. Instituut voor Epilepsiebestrijding, Meer en Bosch, Achterweg 5, Heemstede, The Netherlands **Sodium valproate: serial monitoring of EEG and serum levels.** Neurology. 29(11):1450-1459, 1979.

Serial EEG and serum level monitoring studies were performed on four patients treated with sodium valporate for refractory seizures. All had frequent clinical seizures and generalized spike wave discharges. Valproate appeared to reduce diurnal paroxysmal discharges (PD) and clinical seizures, but was less effective on nocturnal PD. Valproate concentrations fluctuated widely over 24 hours, and peak serum concentrations above 100mcg/ml were necessary in some cases to achieve clinical and EEG improvement. Alterations in the distribution of the total daily dose of valproate appeared to change the pattern of clinical seizures and PD. 13 references. (Author abstract modified)

004615 Satterfield, James H.; Satterfield, Breena T.; Cantwell, Dennis P. Gateways Hospital, Los Angeles, CA **Long-term effects of combined treatments in MBD children.** Psychopharmacology Bulletin. 16(2):64-66, 1980.

One and 2 year outcome evaluations of 61 hyperactive children who participated in a 3 year study of a multimodality treatment program are reviewed. In addition to medication, the hyperactive children received individual and group therapy as well as individual educational therapy for the child, and individual and group therapy for parents, parent training, and family therapy. The results offer some reason for optimism in the treatment outcome of hyperactive children. Behavior was significantly improved in all areas compared to the child's initial status. Improvement in psychosocial adjustment was also demonstrated in the psychiatrist's ratings of adjustment of the children in six areas. 10 references.

004616 Satterfield, James H.; Satterfield, Breena T.; Cantwell, Dennis P. Dept. of Research, Gateways Hospital, 1891 Effie St., Los Angeles, CA 90026 **Multimodality treatment: a two-year evaluation of 61 hyperactive boys.** Archives of General Psychiatry. 37(8):915-919, 1980.

Findings at the end of the second year of a 3 year prospective study of 61 hyperactive boys are reported. Individualized multimodality treatment plans commensurate with each child's disabilities were implemented by the staff. Measures of behavior at home and at school, academic performance, delinquent behavior, and emotional adjustment were obtained initially and at the end of each treatment year. The combination of a clinically useful medication in appropirate dosage schedules with relevant psychological treatments simultaneously directed to each of the multiple disabilities was associated with an unexpectedly good outcome at the end of 1 and 2 years. Whether this improvement will be maintained over a longer period of time and whether young adult outcome will be affected needs more investigation. 16 references. (Author abstract)

004617 Simeon, J.; Waters, B.; Resnick, M. Dept. of Psychiatry, University of Ottawa, Royal Ottawa Hospital, Ottawa, Ontario, Canada **Effects of piracetam in children with learning disorders.** Psychopharmacology Bulletin. 16(3):65-66, 1980.

The efficacy and safety of piracetam (2-pyrrolidone acetamide) were assessed in 29 male children with learning disorders. In a double-blind, cross-over trial, the efficacy of piracetam was compared to that of placebo in 29 boys (8 to 14 years old) with learning disabilities. The findings on global behavior and learning were inconclusive. These changes showed a slightly greater variability with piracetam. The parent and teacher ratings, and the neuropsychological tests showed no significant differences between piracetam and placebo. The neuropsychologist's judgments showed trends in favor of piracetam. EEG results suggest psychoactive properties for piracetam. It is hypothesized that the short duration of each treatment phase and possible withdrawal and/or carryover effects may have resulted in the masking of differences between piracetam and placebo. 10 references.

004618 Streifler, M.; Avrami, E.; Rabey, J. M. Municipal and Government Medical Center, Tel Aviv University Medical School, Ichilov Hospital, Tel Aviv, Israel **L-dopa and the secretion of sebum in parkinsonian patients.** European Neurology. 19(1):43-48, 1980.

Sebum secretion was studied in 14 parkinsonian patients before and after 3 months of treatment with L-dopa. An abnormality of sebum secretion was shown to exist in parkinsonism. In seven patients, successfully treated with L-dopa, sebum secretion diminished and its pattern improved. In all patients in whom L-dopa treatment did not result in noticeable clinical changes, there was no significant modification in sebum secretion. No change was observed in the secretion of sebum of five normal control subjects who were given L-dopa for 1 week. 20 references. (Author abstract)

004619 Szerkely, George A.; Caplan, Rochelle; Rotman, Avner. Rotman: Dept. of Membrane Research, Weizmann Institute of Science, Rehovot, Israel **Platelet dopamine uptake in autistic and other psychotic children. Inhibition by imipramine.** Progress in Neuro-Psychopharmacology. 4(2):215-218, 1980.

The dopamine uptake by blood platelets and the inhibition by imipramine of this uptake were investigated in autistic and other psychotic children during a 3 to 4 week period, and a pilot genetic study in three families was undertaken. Results indicate that the dopamine uptake in the autistic group is about 15% to 20% higher than in the psychotic group, and that the dopamine uptake was much lower than the serotonin uptake measured in both groups under the same conditions. This low specificity and efficienty of the dopamine uptake mechanism in human platelets limits both the validity and reliability of the results. 11 references. (Author abstract modified)

004620 Takamatsu, Norimitsu. Dept. of Pediatrics, Tohoku University School of Medicine, 1-1 Seiryo-cho, Sendai, Japan 980 **Difference of serum diphenylhydantoin levels between in cases of taking diphenylhydantoin alone and in cases of taking multiple anti-convulsants in various age groups.** Brain and Nerve. 31(6):561-568, 1979.

The relationship between an oral dose of diphenylhydantoin (DPH) and serum levels of DPH in 163 epileptic children was investigated. The serum level was determined by Solow's method of gas liquid chromatography. The patients were divided into four groups: 1) DPH with or without other anticonvulsants; B) DPH alone; C) DPH plus phenobarbital (PB) with or without primidone (PRM); D) DPH plus other anticonvulsants with or without PB (PRM). Each group was further divided into four subgroups according to age. Significant correlation was found between oral dose and serum level of DPH in most subgroups of A, B, and C. The slopes of regression lines increased progressively with age in all four groups. Under identified dosage it is speculated that the effect of PB in lowering the serum level of DPH is more intense than that of some other anticonvulsants. The results suggest the interference of PB with DPH metabolism when PB is taken on a chronic basis in cases of epilepsy. 27 references. (Journal abstract modified)

004621 Washton, Arnold M.; Resnick, Richard B.; LaPlaca, Robert W. Dept. of Psychiatry, New York Medical College, New York, NY **Clonidine hydrochloride: a non-opiate treatment for opiate withdrawal.** Psychopharmacology Bulletin. 16(2):50-52, 1980.

Two preliminary studies assessing the ability of clonidine hydrochloride to arrest the acute withdrawal discomfort experienced by opiate addicts and to assess the efficacy of daily clonidine in outpatient detoxification from methadone are described. In a partial replication of a study by Gold, Redmond, and Kleber, a single oral dose of clonidine reduced withdrawal rating scores of methadone addicts significantly; all Ss reported dramatic relief of withdrawal distress. Although statements about the utility of clonidine must await controlled studies, there is good reason to believe that abrupt withdrawal from as much as 40mg daily methadone without clonidine would have been unsuccessful in most cases. 1 reference.

004622 Wender, Paul H.; Reimherr, Frederick W.; Wood, David R. Dept. of Psychiatry, University of Utah College of Medicine, Salt Lake City, UT 84132 **Diagnosis and drug treatment of Attentional Deficit Disorder (Minimal Brain Dysfunction) in adults: a replication. (Unpublished paper).** Research Report, NIMH Grant MH-31130, 1979. 41 p.

A replication of an earlier study which dealt with the diagnosis and treatment of Attentional Deficit Disorder (ADD) (Minimal Brain Dysfunction) in adults is presented. Sixty subjects who met provisional operational criteria for Adult ADD were entered in a random assignment, parallel, double-blind trial of placebo and pemoline, a noneuphorigenic psychostimulant drug effective in ADD children. Sixty five percent of the pemoline group and 46% of the placebo group manifested improvement, a difference that was not statistically significant. When the analyses were confined to that subgroup of patients whose parents had described them in the 95th percentile of childhood hyperactivity or when the hyperactivity score was partialled out statistically, pemoline was demonstrably more effective that place-

bo. The psychological and psychiatric characteristics of this group of patients are presented as well as proposed revised operational criteria for Adult ADD. 56 references. (Author abstract)

004623 Whiteley, A.; Signoret, J. L.; Agid, Y.; Lhermitte, F. Signoret: Clinique de Neurologie et de Neuropsychologie, Hopital de la Salpetriere, 47, Bd de l'Hopital, F-75634, Paris Cedex 13, France **/Influence of choline on amnesia in Alzheimer's disease./** Action de la choline sur les troubles mnesiques de la maladie d'Alzheimer. Revue Neurologique. 135(8-9):565-571, 1979.

Eight patients with Alzheimer's disease presenting with memory difficulties and no significant intellectual deterioration were treated with nine grams daily of choline base orally for 3 weeks. Quantitative testing, which evaluated memory capabilities such as learning and recall after delays of one hour and 24 hours, were used before and after the administration of choline. The results of a global statistical analysis did not show any significant differences in the performances obtained before and after choline. However, in two patients recall performance improvement was confirmed clinically. It is suggested that these two patients were suffering from a mild form of Alzheimer's disease. 21 references. (Journal abstract)

004624 Winsberg, B. G.; Hungund, B. L.; Perel, J. M. Long Island Research Institute, Health Sciences Center, State University of New York, Stony Brook, NY 11790 **Pharmacological factors of methylphenidate metabolism in behaviorally disordered children.** Psychopharmacology Bulletin. 16(3):69-71, 1980.

Factors in the disposition of methylphenidate (MP) and its major metabolite ritalinic acid (RA) were investigated via a recently developed analytical procedure in a group of hyperkinetic children, and the protein binding of MP was investigated. Four behaviorally disordered children received MP in doses appropriate to their clinical condition (10 to 20mg), and plasma specimens were obtained from an additional eight children for protein binding determinations. The brief half-life (2.5 hr) of MP in behaviorally disordered children may be explained in part by its low protein binding, which results in a high percentage of free drug being made available for metabolism to pharmacologically inactive metabolites. The therapeutic activity of MP in hyperactive children appears to be due principally to the parent compound. Implications for clinical management are noted. 8 references.

12 PSYCHOTOMIMETIC EVALUATION STUDIES

004625 Bachman, John A.; Benowitz, Neal L.; Herning, Ronald I.; Jones, Reese T. Langley Porter Neuropsychiatric Institute, University of California, San Francisco, CA 94143 **Dissociation of autonomic and cognitive effects of THC in man.** Psychopharmacology. 61(2):171-175, 1979.

The dissociation of autonomic and cognitive effects of tetrahydrocannabinol (TCH) in humans was investigated. Intravenous THC 30 to 44.8 mcg/kg, was administered to four Ss. Each received THC on four occasions preceded by either i.v. saline, atropine sulfate, propranolol, or both drugs together. Heartrates, subjective intoxication and symptom ratings, time productions, and EEG activity were measured. In the absence of autonomic blocking drugs, THC produced characteristic tachycardia, subjective intoxication, and EEG affects. After combined autonomic blockaged, THC had no effect on heartrate, while subjective and EEG changes remained as intense. These findings argue against the hypothesis that the subjective and EEG effects of THC are mediated by autonomic receptors or by interoception of peripheral autonomic actions of THC. 13 references. (Author abstract modified)

004626 Demisch, Lothar; Neubauer, Manfred. Zentrum der Psychiatrie, Klini. Biochem. Lab., Klinikum der Universitat, D-6000 Frankfurt, Germany **Stimulation of human prolactin secretion by mescaline.** Psychopharmacology. 64(3):361-363, 1979.

The effects of oral administration of 5mg/kg mescaline (3,4,5-trimethoxy-beta-phenylethylamine) or its nonhallucinogenic isomer 2,3,4-trimethoxy-beta-phenylethylamine (2,3,4-TMPEA) on human serum prolactin (PRL) and growth hormone (GH) levels were investigated. Mescaline stimulated the secretion of PRL more than fourfold above baseline levels. Peak concentrations were found 90 to 120 munutes after drug intake. Five hours later, serum PRL was still markedly increased. Mescaline also triggered GH secretion. There was no alteration of serum PRL and GH concentrations after intake of the nonhallucinogenic 2,3,4-TMPEA. The finding of stimulation of PRL secretion by a single oral dose of mescaline sufficient to induce hallucinations in man seems to be the first data to support the view that mescaline may act on serotonin receptors in the human brain. 20 references. (Author abstract modified)

004627 Hartnoll, Richard L.; Mitcheson, Martin C.; Battersby, A.; Brown, Geoffry; Ellis, Margaret; Fleming, Philip; Hedley, Nicholas. University College Hospital Drug Dependence Clinic, 122 Hampstead Rd., London NW1 2LT, England **Evaluation of heroin maintenance in controlled trial.** Archives of General Psychiatry. 37(8):877-884, 1980.

Ninety six confirmed heroin addicts requesting a heroin maintenance prescription were allocated to treatment with injectable heroin or oral methadone and progress was monitored for 12 months. It was found that heroin maintains the status quo and that it is associated with a continuing intermediate level of involvement with the drug subculture and criminal activity. Refusal to prescribe heroin while offering oral methadone constituted a more confrontational response and resulted in a higher abstinence rate, but also a greater dependence on illegal sources of drugs for those who continued to inject. Those offered oral methadone tended to polarize toward high or low categories of illegal drug use and involvement with the drug subculture, and were more likely to be arrested during the 12 month followup. No differences between groups occurred in employment, health, or consumption of nonopiate drugs. Refusal to prescribe heroin resulted in a significantly greater dropout from regular treatment. 21 references. (Author abstract modified)

004628 Silbergeld, Ellen K.; Hruska, Robert E. Experimental Therapeutics Branch, NINCDS, 9000 Rockville Pike, Bethesda, MD 20205 **Lisuride and LSD: dopaminergic and serotonergic interactions in the** Psychopharmacology. 65(3):233-237, 1979.

The behavioral effects of lisuride and LSD were investigated particularly as they related to 5-HT function. In addition, the nature of their dopaminergic regulation of the serotonin syndrome was examined. Lisuride and LSD possess both serotonergic and dopaminergic properties. Unlike LSD, lisuride is reported to be nonhallucinogenic. Because of their similar neurochemical properties but dissimilar psychotropic natures, it was of interest to investigate their behavioral effects. Results suggest that dopaminergic modulation of the serotonin syndrome occurs before the serotonin receptor involved in this behavior. Also, the differences between LSD and lisuride may be relevant to their different psychopharmacological properties. 20 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

004629 Blum, Stuart F. Cooper Medical Center, Camden, NJ 08034 **Lithium in hairy-cell leukemia.** New England Journal of Medicine. 303(8):464-465, 1980.

A report of a patient with hairy cell leukemia who had an unequivocal, sustained improvement in hemoglobin concentration and platelet count in response to lithium carbonate, after failure to respond to splenectomy, is presented. The response of this 60-year-old patient expands knowledge of the clinical utility of lithium carbonate in the treatment of patients with hematologic disorders. The improvement in hemoglobin concentration and platelet count noted in the patient suggests that lithium carbonate may stimulate not only granulocytopoiesis but also erythropoiesis and thrombocytopoiesis. 2 references.

004630 Bonham Carter, Susan M.; Reveley, Michael A.; Sandler, Merton; Dewhurst, John; Little, Betsy C.; Hayworth, Jane; Priest, Robert G. Sandler: Institute of Obstetrics and Gynaecology, Queen Charlotte's Maternity Hospital, London W6 0XG, England **Decreased urinary output of conjugated tyramine is associated with lifetime vulnerability to depressive illness.** Psychiatry Research. 3(1):13-21, 1980.

The oral tyramine test was administered to 77 pregnant women at a prenatal clinic to examine its utility as a screening device for a predisposition to psychiatric morbidity, specifically depressive illness. In this group of women, whose psychiatric histories were unknown, those with the lowest output of urinary tyramine (free plus conjugated) following oral tyramine loading had a significantly higher lifetime incidence of depressive illness compared with those with the highest output. As none of the women were suffering from depression at the time of tyramine loading, it seems likely that this decreased excretion of tyramine is associated in some way with vulnerability to depressive illness, whether puerperal or nonpuerperal. 23 references. (Author abstract modified)

004631 Borg, K.-O.; Johnsson, G.; Jordo, L.; Lundborg, P.; Ronn, O.; Welin-Fogelberg, I. Hassle Research Laboratories, S-431 20 Molndal 1, Sweden **Interaction studies between three antidepressant drugs (zimelidine, imipramine and chlorimipramine) and noradrenaline in healthy volunteers and some pharmacokinetics of the drugs studied.** Acta Pharmacologica et Toxicologica. 45(3):198-205, 1979.

The effects of oral zimelidine (100mg), chlorimipramie (50mg), and imipramine (25mg) were compared in human volunteers. Imipramine potentiated the effects of noradrenaline (NA) infusion on diastolic blood pressure, but zimelidine did not. Chlorimipramine potentiated the effects of NA infused 6 hours later, but not when NA was infused 90 minutes after drug intake. No anticholinergic effects, measured as blockade of salivary secretion, were observed after any of the three drugs. Peak plasma concentration of zimelidine was obtained 2 hours after oral administration; half-life was estimated to be about 7 hours and bioavailability was about 20% of the administered dose. The metabolite desmethylzimelidine was present in plasma in concentration similar to that of the parent drug up to 8 hours after administration and thereafter in significantly higher amounts. The absorption of imipramine and chlorimipramine from the gastrointestinal tract was slow, with peak plasma concentration obtained as late as 6 hours after the drugs were given; the two compounds were eliminated at about the same rate, both more slowly than zimelidine. 30 references. (Author abstract modified)

004632 Bowdle, T. Andrew; Levy, Rene H.; Cutler, Ralph E. Levy: Dept. of Pharmaceutical Sciences, School of Pharmacy, University of Washington, Seattle, WA 98195 **Effects of carbamazepine on valproic acid kinetics in normal subjects.** Clinical Pharmacology and Therapeutics. 26(5):629-634, 1979.

To determine the effect of carbamazepine on valproic acid kinetics, valproic acid (250mg twice daily for 4 weeks) was given orally to six normal Ss and carbamazepine (200mg/day) was begun after 4 days on valproic acid. Minimum steady-state concentrations of valproic acid declined after carbamazepine from 34.4 to 27.1mcg/ml. Clearance rose form 6.46 to 8.48ml/kg/hour. The increase in clearance and decrease in minimum steady-state levels was apparent only after 2 weeks on carbamazepine. The elimination rate constant during the dosing interval did not rise during carbamazepine administration, which suggests the distribution volume may have increased. 32 references. (Author abstract modified)

004633 Briley, M. S.; Langer, S. Z.; Raisman, R.; Sechter, D.; Zarifian, E. Dept. of Biology, Laboratoires d'Etudes et de Recherches Synthelabo, F-75013 Paris, France **Tritiated imipramine binding sites are decreased in platelets of untreated depressed patients.** Science. 209(4453):303-305, 1980.

The high affinity binding of tritiated imipramine to platelet membranes was compared in samples from 16 untreated depressed women and 21 age matched control Ss of the same-sex. The maximal binding in the depressed group was significantly lower than that of the controls, although the affinity constants were similar. These results suggest that binding of triated imipramine in human platelets may represent a biochemical index of depression, possibly reflecting similar changes in the brain. 13 references. (Author abstract)

004634 Brunswick, David J.; Amsterdam, Jay D.; Mendels, Joseph; Stern, Stephen L. VA Hospital, University and Woodland Avenue, Philadelphia, PA 19104 **Prediction of steady-state imipramine and desmethylimipramine plasma concentrations from single-dose data.** Clinical Pharmacology and Therapeutics. 25(5, Part 1):605-610, 1979.

Tricyclic antidepressant plasma levels were measured in patients and in healthy Ss after a single dose of desmethylimipramine (DMI) or imipramine (IMI) and after chronic dosing to steady-states. Tricylic plasma levels measured 24 hours after the single oral dose correlated with steady-state plasma levels. The correlation coefficient was 0.97 between 24 hours and steady-state total tricyclic levels in normal Ss given IMI. Results suggest that the therapeutic dose regimen for tricyclic antidepressants can be calculated on the basis of 24 hours plasma drug levels. 27 references. (Author abstract modified)

004635 Caldara, R.; Ferrari, C.; Barbieri, C.; Romussi, M.; Rampini, P.; Telloli, P. 2a Divisione Medica, Ospedale Fatebenefratelli, Corso di Porta Nuova 23, I-20121 Milan, Italy **Effect of two antiserotoninergic drugs, methysergide and metergoline, on gastric acid secretion and gastrin release in healthy man.** European Journal of Clinical Pharmacology. 17(1):13-18, 1980.

The effects of acute oral administration of the antiserotoninergic drugs methysergide and metergoline on basal, submaximal, and maximal pentagastrin stimulated gastric acid secretion, as well as on basal and food induces gastrin release, were evaluated in healthy volunteers. Methysergide significantly increased basal and submaximal pentagastrin stimulated gastric acid secretion, and metergoline significantly inhibited gastric acidity in all experiments. Basal and stimulated serum gastrin concentrations were not modified by either drug. The effect of methysergide on gastric acid secretion was opposed to that of serotonin and was probably dependent on its antiserotoninergic action, but the decrease in gastric acidity caused by metergoline is not easily explained. Although the effect is similar to that of a dopamine infusion, it does not depend on dopamine receptor stimulation, since it is not influenced by pretreatment with metoclopramide. It is suggested that it might be due to the weak anticholinergic and/or antihistaminic properties of metergoline. 32 references. (Author abstract)

004636 Cohen, Robert M.; Campbell, Iain C.; Cohen, Martin R.; Torda, Tichomir; Pickar, David; Siever, Larry J.; Murphy, Dennis L. Clinical Neuropharmacology Branch, NIMH, NIH Clinical Center 103D41, Bethesda, MD 20205 **Presynaptic noradrenergic regulation during depression and antidepressant drug treatment.** Psychiatry Research. 3(1):93-105,1980.

A specific testable hypothesis in which the supersensitive alpha-2-adrenoreceptors play an important role in the etiology and main maintenance of affective illness is presented based on the following observations: 1) published findings of changes in adrenergic receptors in the periphery and brains of rats in response to antidepressant regimens; 2) new studies of the monoamine oxidase type-A inhibiting antidepressant clorgyline, specifically relating to adaptation in the alpha-adrenergic presynaptic negative feedback system; 3) human peripheral alpha-adrenergic receptor changes from studies of patients with affective illness; and 4) observations from animals and humans experiencing stress and withdrawal from chronic amphetamine and opiate administration, suggesting that the development of supersensitive alpha-2-adrenoreceptors may lead to affective illness in vulnerable individuals. Old and new pharmacologic treatments are discussed in terms of their capacity to specifically alter adrenergic receptor state. 93 references. (Author abstract)

004637 Collins, John; Evans, Bradley D.; Vogel, Wolfgang H. Dept. of Pharmacology, Jefferson Medical College, Philadelphia, PA Psychopharmacology Bulletin. 16(2):12-14, 1980.

Clinical and experimental studies of various high potency and low potency antipsychotic drugs are reviewed in relation to factors such as absorption, penetration of the blood-brain barrier (BBB), excretion, therapeutic levels, etc. Based on the results of these studies, it is concluded; 1) that the clinical dose in humans seems to be higher than the dose which interferes with the conditioned avoidance response (CAR) in rats; 2) that no correlation or trend is seen in plasma levels of rat and man which could be indicative of a species difference; 3) that most drugs penetrate well into the brain and actually seem to be concentrated in the DNS against a concentration gradient except chlorprothixene; 4) that in rats, brain levels increase generally with increasing doses, indicating that doses seem to reflect brain levels; 5) that no clear correlation exists between inhibition of dopamine binding and the effective brain levels in rats; and 6) that brain levels of antipsychotic drugs necessary to interfere with the CAR range from 0.04 to 3.2 nmoles/g. 10 references.

004638 Czernik, Adelheid; Kleesiek, K. Abt. Psychiatrie, Medizinische Fakultat, RWTM Aachen, D-5100 Aachen, Germany / **Neuroendocrine changes in long-term therapy with lithium salts./** Neuroendokrinologische Veranderungen unter Langzeitbehandlung mit Lithiumsalzen. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(4):305-312, 1980.

Neuroendocrinological changes associated with long-term lithium therapy were investigated in 15 recurrent endogenous depressive or manic-depressive patients, free of psychotic symptoms and under lithium prophylaxis for about 3.9 years, and in 16 sex matched healthy control of approximately the same age. Subjects were administered 0.1 U insulin/kg, 200 mcg thyrotropin releasing hormone, and 50 mcg luteinizing hormone releasing hormone. Human growth hormone (HGH), thyrotropin stimulating hormone (TSH) prolactin (PRL), follicle stimulating hormone (FSH), luteinizing hormone (LH), and cortisol were examined prior to stimulation and 20, 30, 45, 60, and 90 min postadministration. PRL, FSH, and LH did not show any effect under lithium salts. All patients under lithium showed elevated TSH levels under basal conditions and after stimulation compared to controls. This difference was highly significant for younger, premenopausal women. Men and premenopausal women had significantly higher HGH levels after stimulation relative to controls. Postmenopausal women did not show the effect of lithium on HGH levels. 33 references. (Journal abstract modified)

004639 Dubb, J. W.; Stote, R. M.; Alexander, F.; Intoccia, A. P.; Geczy, M.; Pendleton, R. G. Presbyterian-University of Pennsylvania Medical Center, 51 N. 39th St., Philadelphia, PA 19104 **Studies with a PNMT inhibitor.** Clinical Pharmacology and Therapeutics. 25(6):837-843, 1979.

The effects of 7,8-dichloro-1,2,3,4-tetrahydroisoquinoline hydrochloride (DCTQ), a potent inhibitor of phenylethanolamine N-methyltransferase (PNMT), were studie in 23 healthy male Ss. Plasma drug levels up to 6.26mcg/ml were readily obtained following oral administration of DCTQ. There were few subjective and no objective clinical changes. DCTQ did not alter blood pressure or resting plasma and urinary catecholamine levels. No CNS symptoms were observed. Results indicate that acute inhibition of PNMT under resting conditions has no significant clinical effect. 28 references. (Author abstract modified)

004640 Emrich, H. M.; v. Zerssen, D.; Moller, H.-J.; Kissling, W.; Cording, C.; Schietsch, H. J.; Riedel, E. Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 10, D-8000 Munich 40, Germany **Action of propranolol in mania: comparison of effects of the d- and the l-stereoisomer.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(4):295-304, 1980.

The antimanic action of high doses of the beta-receptor blocking agent, propranolol, was investigated in eight psychiatric patients, using a double-blind, placebo controlled ABA design. For comparison, the d-stereoisomer (which is practically devoid of beta blocking action) was used. Six trials were performed with d-propranolol, six trials with the racemic mixture. It was found from dose response relationships that the d-stereoisomer was about half as effective against manic syndromes as the racemic (dl-propranolol) mixture. This suggests that the antimanic action of dl-propranolol is at least partly due to a mechanism independent of the beta blocking action of l-propranolol. Possible mechanisms are discussed including the membrane stabilizing effect of propranolol and a GABA mimetic effect of propranolol. 45 references. (Author abstract modified)

004641 Extein, Irl; Pottash, A. L. C.; Gold, Mark S.; Sweeney, Donald R.; Martin, David M.; Goodwin, Frederick K. Fair Oaks Hospital, 19 Prospect St., Summit, NJ 07901 **Deficient prolactin response to morphine in depressed patients.** American Journal of Psychiatry. 137(7):845-846, 1980.

Endogenous opioid systems of depressed patients were studied using a neuroendocrine challenge paradigm, and the deficient prolactin response to morphine of depressed patients was investigated. Morphine infusion in normal volunteers (n=2) and personality disorder inpatients (n=4) produced significant increases in serum prolactin 30, 60, 90, 120, and 180 minutes after infusion, while for patients with major depressive disorder (n=10), only small, nonsignificant increases in serum prolactin were observed. It is suggested that the absent or blunted responsivity to morphine challenge may reflect abnormalities in central endorphin, dopamine, serotonin, or other neuroregulatory systems (including possible opioid receptor deficits, excess endogenous opioid antagonists, or elevated endorphin levels with compensatory regulation of opioid receptors). 10 references.

004642 Frazer, Alan. Veterans Administration Hospital, Philadelphia, PA **Antidepressant drugs: effect on adrenergic responsiveness and monoamine receptors.** Psychopharmacology Bulletin. 16(3):77-78, 1980

The effects of adrenergic responsiveness and monoamine receptors of antidepressant drugs are discussed, and implications of recent studies for etiological theories of affective illnesses are noted. Data are reviewed which indicate that both acute and chronic desmethylimipramine administration reduce adrenergic responsivenss, and that antidepressant drugs produce complex, and perhaps different, secondary effects on monoamine containing neuronal systems. There appear to be differences in the compensatory mechanisms of individual monoamine systems, and there are important and complex interactions between different biogenic amine systems which may affect the net outcome of antidepressant drug treatment. It is contended that a proper understanding of the mode of action of these drugs, which might provide some insight into the etiology of affective illnesses, will have to encompass an integrated understanding of all these effects over the time course of treatment and clinical response. 12 references.

004643 Froscher, W. Universitats-Nervenklinik Bonn, Neurologie/Epileptologie, Sigmund-Freud-Str 25, D-5300 Bonn 1-Venusberg, Germany /**Clinical significance of blood level determinations of antiepileptic drugs.**/ Klinische Relevanz von Blutspiegeluntersuchungen bei der Therapie mit Antiepileptika. Fortschritte der Neurologie-Psychiatrie und ihrer Grenzgebiete. 48(5)270-293, 1980

Studies are reviewed on the clinical significance of blood level determinations of antiepileptic drugs. The results of the studies have been contradictory and inconclusive. However, in general, blood level determinations are regarded as valuable if the drug has been ineffective for unknown reasons. Indications for blood level determinations include suspected irregular compliance, dosage control, dosage reduction, intoxications, evaluation of unspecific complaints, and the determination of drug interactions. 77 references. (Journal abstract modified)

004644 Ghose, Karabi. Lingfield Hospital School, St. Piers Lane, Lingfield, Surrey RH7 6NX, England **Decreased tyramine sensitivity after discontinuation of amitriptyline therapy.** European Journal of Clinical Pharmacology. 18(2):151-157, 1980.

The pharmacodynamic half-life (Pd1/2) of amitriptyline (AT) was studied in six depressed patients treated with 150mg of AT as a single oral dose for 6 or more weeks. Decreased tyramine sensitivity (DTS), an index of this drug's pharmacological activity, was determined serially at various intervals after the last dose. Plasma concentrations of AT and nortriptyline (NT) were also estimated. It was possible to detect DTS for 228 to 230 hr after the last oral dose and the mean Pd1/2 of this decline of pharmacodynamic effect was observed to be 135 hr. The pharmacokinetic parameters of NT were directly related to those of AT. Prolonged pharmacodynamic effects of this drug after discontinuation should be borne in mind to avoid drug interactions and autonomic complications, expecially after overdosage. It is noted that the DTS test can be used as an alternative technique to assess the biological activity of a drug which inhibits noradrenaline reuptake mechanisms and/or blocks alpha-adrenoceptors at the peripheral neuronal sites. 32 references. (Author abstract modified)

004645 Glaeser, Bruce S.; Melamed, Eldad; Growdon, John H.; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Elevation of plasma tyrosine after a single oral dose of L-tyrosine.** Life Sciences. 25(3):265-271, 1979.

Plasma tyrosine concentrations in 12 normal, fasting human subjects were significantly elevated 2 to 8 hours after ingestion of 100 or 150mg/kg tyrosine. Mean plasma tyrosine levels were maximal after 2 hours, rising from 69 to 154nM/ml after the 100mg/kg dose and to 203nM/ml after the 150mg/kg dose. The mean ratio of plasma tyrosine concentration to the sum of the concentrations of six other neutral amino acids that compete for the same blood-brain barrier uptake system increased from 0.10 to 0.28 2 hours after the 100mg/kg dose and to 0.35 after the 150mg/kg dose. No side-effects of orally administered L-tyrosine were noted. 18 references. (Author abstract modified)

004646 Glass, Allan R.; Schaaf, Marcus; Dimond, Richard C. Kyle Metabolic Unit, Walter Reed Army Medical Center, Washington, DC 20012 **Amitriptyline-induced suppression of growth hormone in acromegaly.** Psychoneuroendocrinology. 5(1):81-86, 1980.

The effect of amitriptyline on the production of growth hormone was studied in five acromegalic patients who had persistent elevations of growth hormone despite prior surgery and radiotherapy. Amitriptyline administered at 100mg p.o. daily at bedtime for 1 month significantly reduced 24 hour mean serum growth hormone in three of the patients (44%, 22%, and 18% reductions). Suppression of growth hormone occurred primarily in the late afternoon and evening, and the usual nocturnal rise in serum growth hormone was delayed. It is suggested that the clinical usefulness of amitriptyline in treating acromegaly is probably very limited because of the modest nature of the reductions in serum growth hormone. 13 references. (Author abstract modified)

004647 Gold, Philip W.; Extein, Irl; Pickar, David; Rebar, Robert; Ross, Richard; Goodwin, Frederick K. Unit on Neuroendocrinology, Clinical Psychobiology Branch, NIMH, 9000 Rockville Pike, Bldg. 10, Rm. 4S239, Bethesda, MD 20205 **Suppression of plasma cortisol in depressed patients by acute intravenous methadone infusion.** American Journal of Psychiatry. 137(7):862-863, 1980.

The effects of exogenous opiate administration on hypothalamic/pituitary/adrenal (HPA) axis function in patients with a major depressive disorder were investigated, and the suppression of plasma cortisol in depressed patients by acute intravenous methadone infusion was examined. The suppression of cortisol secretion in four research diagnostic criteria depressed Ss by methadone infusion is interpreted as reflecting negative feedback effects exerted on corticotropin releasing factor (CRF) and/or adrenocorticotropin (ACTH) secretion via opiate receptors located at hypothalamic and pituitary levels. If methadone suppresses cortisol levels via feedback inhibition of CRF and/or ACTH, it may be possible to devise a methadone suppression test, analogous to the dexamethasone suppression test, to evaluate the set point for feedback inhibition exerted by opiates on the HPA, and to explore the possible relationship between endogenous opiate function and HPA activation in depressed patients. 10 references.

004648 Goodnick, Paul J.; Evans, Hugh E.; Dunner, David L.; Fieve, Ronald R. Dept. of Psychiatry, Wayne State University, V.A. Medical Center, Southfield and Outer Drive, Allen Park, MI 48101 **Amino acid concentrations in cerebrospinal fluid: effects of aging, depression, and probenecid.** Biological Psychiatry. 15(4):557-563, 1980.

Cerebrospinal fluid (CSF) amino acid concentrations were measured in six Bipolar I, eight Bipolar II, eight Unipolar, and four other and control patients. All but four were also studied after administration of probenecid. Fourteen amino acids showed significant correlations of concentrations with age of subjects. Significant diagnostic group differences were found for five amino acids; only that of tyrosine persisted after taking subject's age into account. Following probenecid administration,

there were statistically significant changes in CSF concentration of several amino acids, but these changes were small and likely indicative of diurnal changes. 19 references. (Author abstract)

004649 Greenblatt, David J.; Shader, Richard I. Massachusetts General Hospital, Boston, MA 02114 **Kinetics of diazepam and lorazepam in the elderly.** Psychopharmacology Bulletin. 16(2):56-57, 1980.

Gender dependent and age dependent variations in the kinetics of two benzodiazepine derivatives, diazepam and lorazepam, were investigated in two studies. A series of young (19 to 38 years) and elderly (aged 61 to 84 years) volunteers received single intravenous doses of diazepam and/or lorazepam, and kinetic properties were determined from drug concentrations measured by electron capture, gas liquid chromatography. Results indicate that even within the same drug class, the effect of age on drug disposition and clearance may be influenced by physicochemical properties and the metabolic pathway of the particular drug, as well as by the S's gender. 3 references.

004650 Hoffer, A. 3-A, 2727 Quadra Street, Victoria B. C., Canada V8T 4E5 **Allergy, depression and tricyclic antidepressants.** Journal of Orthomolecular Psychiatry. 9(3):164-170, 1980.

The clinical and experimental research literature which supports the conclusions that a large fraction of depressions are allergenic responses to environmental molecules, and that the tricyclic antidepresssants are effective in many patients because of their antihistaminic properties, not because they act upon the serotonin or sympathomimetic amine pathways, is reviewed. Three lines of evidence concerning the hypothesized mechanisms of action of the tricyclic antidepressants are reviewed: 1) the close association between depression and allergies; 2) manserine, a powerful antidepressant and antihistamine, differs from the tricyclics in having no effect on the metabolism in the brain of catecholamines or serotonin; and 3) tricyclic antidepressants are useful in treating allergic reactions ranging from obesity to enuresis. Other topics discussed include: depression as an allergic reaction; and treatment of food allergy by tricyclic antidepressants. 18 references.

004651 Inagawa, Tetsuji; Kajikawa, Hiroshi; Kodama, Motomu; Ishikawa, Susumu; Oozumi, Tohru. Dept. of Neurosurgery, Shimane Prefectural Central Hospital, Izumo, Japan **Histochemical studies on the uptake of exogenous monoamines and their precursors in the rat brain.** Brain and Nerve. 32(3):281-291, 1980.

The uptake of monoamines (MA) and their precursors in the brain were studied after their intraperitoneal and intraventricular injection into normal, reserpine or reserpine-nialamide pretreated rats, using the histochemical fluorecence method of Falck and Hillarp. After intraperitoneal injection of L-Dopa or L-5-HTP, a fluorescence was observed in the endothelial cells and pericytes of the capillaries, but not after domapine (DA) or 5-HT. After intraperitoneal injection of L-Dopa, the fluorescence intensity of DA neurons was increased, and after intraventricular injection of L-Dopa, 5-HT cell bodies as well as DA neurons showed an accumulation of green fluorescence. Additional findings are considered, which have implications concerning the therapeutic and side-effects of high doses of L-Dopa. 44 references. (Journal abstract modified)

004652 Kaiya, Hisanobu. Dept. of Neuropsychiatry, Gifu University School of Medicine, Gifu, Japan **Neuromelanin, neuroleptics and schizophrenia: hypothesis of an interaction between noradrenergic and dopaminergic system.** Neuropsychobiology. 6(5):241-248, 1980.

Neuromelanin was measured microspectrophotometrically in the substantia nigra and the locus ceruleus of 12 brains of schizophrenia patients who had undergone neuroleptic therapy to evaluate the assumption that neuromelanin content indicates neuronal activity in the catecholaminergic system. Neuromelanin increased with age in both regions of 40 control brains. Although no significant difference in melanin content between medicated and control brains was seen, a high negative correlation was noted in melanin content between the substantia nigra and the locus ceruleus only in each medicated brain, especially in cases of schizophrenia. The possibility of noradrenergic and dopaminergic interaction is discussed. 29 references. (Author abstract modified)

004653 Kalin, Ned H.; Risch, Samuel C.; Cohen, Robert M.; Insel, Thomas; Murphy, Dennis L. Clinical Neuropharmacology Branch, NIMH, Bethesda, MD 20205 **Dexamethasone fails to suppress beta-endorphin plasma concentrations in humans and rhesus monkeys.** Science. 209(4458):827-828, 1980.

In humans and rhesus monkeys, dexamethasone was found to decrease concentrations of plasma cortisol but not to alter circulating beta-endorphin immunoreactivity. Contrary to current theory suggesting that pituitary beta-endorphin and adrenocorticotropic hormone are controlled by identical regulatory mechanisms for synthesis and release, these results suggest that in higher primates, the established glucocorticoid feedback mechanisms for the adrenocorticotropic hormone/cortisol system does not regulate beta-endorphin secretion in the same way. 14 references. (Author abstract modified)

004654 Kalow, W.; Tang, B. K.; Kadar, D.; Endrenyi, L.; Chan, F.-Y. Dept. of Pharmacology, Medical Sciences Building, University of Toronto, Ontario, Canada M5S 1A8 **A method for studying drug metabolism in populations: racial differences in amobarbital metabolism.** Clinical Pharmacology and Therapeutics. 26(6):766-776, 1979.

The amobarbital metabolites 3'-hydroxyamobarbital (C-OH) and 1-(beta-D-glucopyranosyl) amobarbital (N-glu) were determined in urine samples from Caucasian and Oriental Ss. The average concentration of C-OH was greater in Caucasians than in Orientals, and the reverse was true for the N-glu metabolite. A trend toward more N-glu metabolite in urine of females than of males was also noted. Measuring the metabolite/creatinine ratios narrowed the distribution range of the data, but population differences were not changed. 29 references. (Author abstract modified)

004655 Kangas, L. Dept. of Pharmacology, Turku University, Kiinamyllynkatu 10, SF-20520 Turku 52, Finland **Urinary elimination of nitrazepam and its main metabolites.** Acta Pharmacologica et Toxicologica. 45(1):16-19, 1979.

Nitrazepam and its main metabolities, 7-aminonitrazepam and 7-acetamidonitrazepam, were determined in urine following oral administration of 5mg nitrazepam to 15 healthy male volunteers. The determinations were performed by gas/liquid chromatography, using an electron capture detector for unchanged nitrazepam and a nitrogen selective detector for the metabolites. Unchanged nitrazepam was poorly eliminated through the kidneys (about 1% of the dose). The interindividual variation of total excreted urinary metabolites was large, ranging from 848 to 4,933mcg or from 17 to 99% of the dose over 7 days. Conjugated metabolites made up 57% of total metabolites excreted in urine. The urinary half-lives were 44 and 46 hours for free and conjugated 7 aminonitrazepam and 12 and 18 hours for free and conjugated 7-acetamidonitrazepam. The half-lives of the excreted amounts of the metabolites did not correlate with any phar-

macokinetic parameter of unchanged nitrazepam in serum. 5 references. (Author abstract modified)

004656 Kangas, L.; Allonen, H.; Lammintausta, R.; Salonen, M.; Pekkarinen, A. Research Center, Farmos Group Ltd. PO Box 425, SF-20101 Turku 10, Finland **Pharmacokinetics of nitrazepam in saliva and serum after a single oral dose.** Acta Pharmacologica et Toxicologica. 45(1):20-24, 1979

The pharmacokinetics of nitrazepam in saliva and serum were studied in 12 male volunteers after oral administration of 5mg nitrazepam. Concentrations of nitrazepam in serum and saliva were significantly correlated, but concentrations in saliva were significantly lower than the protein unbound fraction in serum. Peak concentrations were 40.7ng/ml in serum 2.4 hours after administration and 1.9ng/ml in saliva 2.5 hours after dosing. The mean half-life of nitrazepam was 30.5 hours in serum and 39.9 hours in saliva. It is concluded that analysis of nitrazepam concentrations in saliva has neglible clinical value. 32 references. (Author abstract modified)

004657 Koulu, M.; Lammintausta, R.; Kangas, L.; Dahlstrom, S. Dept. of Pharmacology, Institute of Biomedicine, University of Turku, Kiinamyllynkatu 10, SF-20520 Turku 52, Finland **The effect of methysergide, pimozide, and sodium valproate on the diazepam-stimulated growth hormone secretion in man.** Journal of Clinical Endocrinology & Metabolism. 48(1):119-122, 1979.

The neuroendocrinological effect of diazepam on human GH (hGH) secretion was investigated to determine the role of dopaminergic, serotonergic, and GABA-ergic mechanisms. Diazepam induced GH secretion was tested on 28 male volunteers before and after a 3 day treatment with methysergide, pimozide, or sodium valproate. Serum GH, diazepam, and blood glucose levels were determined. Without prior medication, the mean serum GH level increased 336% 1 hour after diazepam administration. Treatment with the serotonin antagonist, methysergide, had no effect on the diazepam stimulated GH secretion, whereas pimozide, the selective dopamine recptor blocking agent, reduced the GH response to diazepam by 50%. Sodium valproate, a gamma-aminobutyric acid transaminase inhibitor, also inhibited diazepam induced GH secretion; stimulated GH levels were 51% at 30 minutes, 39% at 60 minutes, and 46% at 90 minutes relative to the stimulated levels without medication. No difference was found in blood glucose or serum diazepam levels after the drug treatments relative to the values obtained under basal conditions. It is suggested that diazepam induced GH secretion is at least partly mediated via dopaminergic mechanisms. Serotonin does not seem to be involved. It is further proposed that gamma-aminobutyric acid plays an inhibitory role in GH secretion. 17 references. (Author abstract)

004658 Krause, K.-H.; Schmidt-Gayk, H.; Gutscher, D.; Gutscher, G. Neurologische Universitatsklinik, Vossstr. 2., D-6900 Heidelberg, Germany **/Serum folic acid in anticonvulsant long-term therapy./** Serumfolsaurespiegel unter antiepileptischer Langzeittherapie. Archiv fur Psychiatrie und Nervenkrankheiten. 228(1):91-94, 1980.

The values of unreduced serum folic acid in 48 epileptics treated with hydantoin and 38 controls were compared using a competitive protein binding assay. No significant differences were found. The average folic acid value was 7.73 mcM/l in epileptics, a little higher than the 7.18 mcM/l found in controls. This supports the hypothesis that the folate deficiency in epileptics is caused by blocking the conversion of folic acid to 5-methyltetrahydrofolic acid by phenytoin. 21 references. (Journal abstract modified)

004659 Kupfer, David J.; Hanin, Israel; Spiker, Duane G. Dept. of Psychiatry, Western Psychiatric Institute and Clinic, Pittsburgh, PA **EEG sleep and tricyclic plasma levels in primary depression.** Psychopharmacology Bulletin. 16(2):35-36, 1980.

EEG sleep and tricyclic plasma levels in primary depression were investigated among 25 patients. Plasma levels of amitriptyline (AMI) were found to be correlated significantly and consistently with the tonic aspects of REM sleep, while REM sleep variables showing the greatest level of tolerance to drug administration (i.e., phasic components of REM sleep) showed no significant relationships to plasma AMI levels. Although the administration of AMI is associated with rapid and widespread effects on the sleep patterns of depressed patients, the REM cycle or the initiation of REM sleep appears to be selectively correlated with concurrent tricyclic plasma levels. Nortriptyline (NT) levels show similar correlations, although it appears that the AMI plasma levels may be more specifically related to the REM sleep variables. Since AMI has a more pronounced anticholinergic effect than does NT, these findings are consistent with the available data demonstrating a correlation between cholinergic activation and REM sleep initiation. 4 references.

004660 Leckman, James F.; Maas, James W.; Redmond, D. Eugene, Jr.; Heninger, George R. Dept. of Psychiatry, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510 **Effects of oral clonidine on plasma 3-methoxy-4-hydroxyphenethyleneglycol (MHPG) in man: preliminary report.** Life Sciences. 26(25):2179-2185, 1980.

Repeated (N=15) administration of clonidine to three normotensive male Ss was found to cause significant decreases in plasma free 3-methoxy-4-hydroxyphenethyleneglycol (MHPG) at 3 hr for both the 1microgram/kg dose and the 5microgram/kg dose when compared to concentrations following placebo. The mean decrement in plasma free MHPG following a 5microgram/kg dose was 36%. Systolic blood pressure fell a mean of 17 mmHg after 1microgram/kg and 37 mmHg after 5microgram/kg of clonidine. The application of a clonidine challenge test to assess noradrenergic receptor sensitivity in vivo is discussed. 43 references. (Author abstract)

004661 Legros, J. J. Dept. of Clinical and Medical Pathology, CHU, B-23, University of Liege, Sart Tilman, B-4000 Liege, Belgium **The neurohypophyseal peptides: biosynthesis, biological role and prospects of use in neuropsychiatric therapy.** Triangle. 18(1):17-30, 1979.

The cerebral and behavioral effects of the two major neurohypophyseal nonapeptides are described. Recent research indicates that the biosynthesis of the peptides commences with a precursor of high molecular weight and the possible release of other peptides characterized by physiological and psychological actions which are not well defined. The use of these peptides may be envisaged either for substitution therapy in patients in whom a deficiency of neuropeptide secretion has been demonstrated or for pharmacological therapy. The perfection of structural analogues of the neurohypophyseal peptides free from certain undesirable physiological actions should result in a wider scope for their use in therapy. 98 references.

004662 Lieberman, K. W.; Stokes, P. Dept. of Psychiatry, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Entry of lithium into erythrocytes.** Research Communications in Psychology, Psychiatry, and Behavior. 5(2):231-234, 1980.

The entry of lithium into erythrocytes was examined with 19 affective disorder patients and 31 normal control subjects. The rate of entry of lithium ion into erythrocytes obtained from affective disorder females is less than into erythrocytes from normal and affective disorders males and normal females. Implications are that some factors responsible for governing ion

transport across cell membranes may be related to the etiology of affective disorders. 8 references. (Author abstract modified)

004663 Lieberman, K. W.; Stokes, P. Psychobiology Study Unit, Dept. of Psychiatry, Cornell University Medical College, 1300 York Ave., New York, NY 10021 **Lithium distribution ratios in psychiatrically normal subjects.** Pharmacology Biochemistry and Behavior. 13(2):205-208, 1980.

Intracellular (erythrocyte) and extracellular (plasma) electrolytes were studied in six psychiatrically normal Ss treated with lithium carbonate three times a day for 11 days. Intracellular sodium and potassium were reduced throughout the lithium treatment period; the greatest drop in potassium was seen during the first 4 days of treatment, but the reduction in sodium varied from day to day. No comparable alteration in plasma electrolytes was observed. Plasma lithium levels stabilized on day 3 and erythrocyte lithium levels stabilized on day 7. The erythrocyte/plasma ratio on days 7 through 11 maintained a constant value of 0.35, which is lower than that reported for patients with affective disorders. 33 references. (Author abstract modified)

004664 Lingjaerde, Odd. Dept. of Clinical Psychiatry, University of Tromso, Tromso, Norway **Inhibitory effect of clomipramine and related drugs on serotonin uptake in platelets: more complicated than previously thought.** Psychopharmacology. 61(3):245-249, 1979.

Complexities of the inhibitory effect of clomipramine and related drugs on serotonin uptake in platelets of healthy unmedicated volunteers were investigated. The use of an adequate blind value and correction for rapid decrease in substrate concentration during the incubation are emphasized. Pure competitive inhibition was found for imipramine and desmethylchlomipramine, with increased Michaelis' constant (Km) without change in maximal uptake rate (Vmax). Clomipramine, and to a lesser degree, the new compound citalopram also reduce Vmax, indicating a mixed competitive and noncompetitive inhibitory effect, even at extremely low concentrations. The noncompetititve component of the clomipramine inhibition is not significantly influenced by increasing the period of preincubation, by varying pH, or by increasing the concentration of potassium. Contrary to desmethylclomipramine, however, clomipramine seems to interfere with the effect of chloride in the uptake process, by blocking the otherwise stimulatory effect of higher concentrations of this anion. 17 references. (Author abstract modified)

004665 Linnoila, Markku; Viukari, Matti; Vaisanen, Kyosti; Auvinen, Juhani. Box 3870, Duke University Medical Center, Durham, NC 27710 **Effect of anticonvulsants on plasma haloperidol and thioridazine levels.** American Journal of Psychiatry. 137(7):819-821, 1980.

The effect of anticonvulsants on plasma haloperidol and thioridazine levels was investigated in a double-blind study employing 30 mentally retarded patients as Ss. Patients who had therapeutic plasma level of phenobarbital and/or diphenylhydantoin had significantly lower plasma levels of haloperidol and mesoridazine, the active metabolite of thioridazine, than patients who did not receive anticonvulsants. Plasma thioridazine levels per se were not affected by concomitant anticonvulsant treatment. Biperiden, an antimuscarinic, antiparkinsonian agent, did not affect the plasma levels of these three neuroleptics. 19 references. (Author abstract modified)

004666 Lund, J.; Lomholt, B.; Fabricius, J.; Christensen, J. A.; Bechgaard, E. Research Laboratories, A/S Ferrosan, DK-2860 Soborg, Denmark **Paroxetine: pharmacokinetics, tolerance and depletion of blood 5-HT in man.** Acta Pharmacologica et Toxicologica. 44(4):289-295, 1979.

The effects of paroxetine, a potent serotonin (5-HT) uptake inhibitor and potential antidepressant, were examined in healthy volunteers after single oral doses of 10, 25, 50, or 75mg and after daily doses of 10, 25, or 50mg for 7 or 14 days. No toxic effects on blood, kidney, liver, heart, or general condition were found in laboratory and clinical examinations. Pharmacokinetic studies revealed dose dependent bioavailability, slow elimination, good fit to a one compartment open model, and almost complete metabolism of the sbustance. The maximal reductionof 5-HT in blood (to about 0.03mcg/ml) was observed within 2 to 3 weeks with a daily dose of 25mg. The 5-HT levels returned to normal within 3 to 4 weeks after paroxetine treatment was terminated. These findings are consistent with preliminary studies in depressed patients, who showed maximal depletion of blood 5-HT within 10 to 12 days on 20mg/day paroxetine. 15 references. (Author abstract modified)

004667 Magnussen, I.; Nielsen-Kudsk, F. University Dept. of Neurology, DK-8000 Aarhus, Denmark. **Pharmacokinetics of intravenously administered L-5-hydroxytryptophan in man.** Acta Pharmacologica et Toxicologica. 44(4):308-314, 1979.

The pharmacokinetics of 5-hydroxytryptophan (5-HTP, 0.2mg/kg i.v.) were studied in five patients pretreated for 1 week with the L-aromatic amino acid decarboxylase inhibitor carbidopa. The plasma concentration/time lapse plot showed biexponential disposition characteristics, and data could be fitted to an open, two compartment pharmacokinetic model, with elimination from the central compartment. The biological half-life of 5-HTP was about 6 hours, the apparent volume of the central compartment was 0.3361/kg, and the plasma clearance was 0.1051/kg/hour. The derived pharmacokinetic constants were successfully used to predict plasma concentrations of 5-HTP during i.v. infusion therapy, but several patients vomited after total doses of 36 to 128mg. 23 references. (Author abstract modified)

004668 Major, Leslie F.; Lake, C. Raymond; Lipper, Steven; Lerner, Pauline; Murphy, Dennis L. Clinical Neuropharmacology Branch, NIMH, NIH Clinical Center 10/3D48, Bethesda, MD 20205 **The central noradrenergic system and affective response to MAO inhibitors.** Progress in Neuro-Psychopharmacology. 3(5/6):535-542, 1979.

The central noradrenergic system and affective response to MAO inhibitors were investigated via analysis of cerebrospinal fluid (CSF) samples obtained from depressed patients before and after treatment with two MAO inhibiting antidepressant drugs, clorgyline and pargyline. Patients were rated twice daily by nursing staff on a modified 15 point scale for severity of global depression and anxiety. Patients were also rated using the Hamilton depression rating scale. High negative correlations were observed between the drug related changes in CSF norepinephrine (NE) and the changes in depression ratings on both the global ratings and the Hamilton scale. Changes in NE were also highly correlated with changes in global anxiety ratings calculated on the basis of changes from baseline for each measurement. Drug related changes in CSF dopamine-beta-hydroxylase similarly showed negative correlations with clinical response. In contrast, no significant correlations were found when drug related changes in CSF 3-Methoxy-4-hydroxy-phenylethylene glycol were compared to changes in clinical state. 42 references. (Author abstract modified)

004669 McEntee, William J.; Mair, Robert G. Neurology Service, Veterans Administration Medical Center, Providence, RI

Korsakoff's amnesia: a noradrenergic hypothesis. Psychopharmacology Bulletin. 16(2):22-24, 1980.

Results of two experimental approaches to delineate the role of monoamine systems in Korsakoff's amnesia (measurement of monoamine metabolites in cerebrospinal fluid; CSF, and study of the effects of monoamine altering drugs on memory and perceptual impairment in Korsakoff patients) are described. Four arguments suggestive of a relationship between Korsakoff's amnesia and noradrenergic mechanisms are cited: 1) the lesions associated with this disease overlap the anatomical locations of ascending noradrenergic pathways; 2) Korsakoff patients show deficits in CSF levels of the primary brain metabolite of norepinephrine, MHPG, and the extent of this deficit correlates with psychometric measures of their memory impairment following treatment with clonidine, a putative alpha-noradrenergic activator; and 4) psychological experiments have demonstrated impaired attention in Korsakoff patients and have suggested that attentional mechanisms may contribute importantly to the memory deficits associated with this disease. 12 references.

004670 Medina, Jose L.; Fareed, Jewed; Diamond, Seymour. Diamond Headache Clinic, Ltd., 5252 N. Western Ave., Chicago, IL 60625 **Lithium carbonate therapy for cluster headache: changes in number of platelets, and serotonin and histamine levels.** Archives of Neurology. 37(9):559-563, 1980.

The utility and therapeutic efficacy of lithium carbonate therapy for cluster headache was investigated. Three groups of patients were studied: Group A consisted of 12 cluster headache patients treated with lithium carbonate; Group B consisted of six cluster headache patients treated with other drugs; and Group C consisted of five patients with muscle contraction headache who received lithium. Serum lithium levels, platelet count, platelet serotonin levels, and platelet rich plasma histamine levels were determined before and during therapy. The frequency of headaches and levels of serotonin and histamine tended to follow a parallel course in Group A and Group B. It is concluded that lithium, by modifying the headache course, changes serotonin and histamine levels. 12 references. (Author abstract modified)

004671 Mohamed, S. N.; Kazarian, S.; Merskey, H.; Thompson, M. G. G. Merskey: Education and Research Dept., London Psychiatric Hospital, 850 Highbury Avenue, London, Ontario N6A 4H1, Canada **Treatment of tardive dyskinesia with dihydrogenated ergot alkaloids (Hydergine): a pilot study.** Canadian Journal of Psychiatry. 25(4):325-328, 1980.

Five patients with abnormal involuntary movements of tardive dyskinesia were treated with dihydrogenated ergot alkaloids (Hydergine) in doses of 3 to 4 mg daily for 6 weeks. Blind ratings of standard videotape recordings indicated significant differences between the patients. Worsening occurred in three patients during treatment and to a lesser extent after treatment; improvement during treatment occurred in one patient and more sustained improvement was found in one patient. 7 references. (Author abstrtact)

004672 Murphy, Dennis L.; Lipper, Steven; Slater, Stanley; Shiling, David. NIH Clinical Center, 10-3D48, Bethesda, MD 20205 **Selectivity of clorgyline and pargyline as inhibitors of monoamine oxidases A and B in vivo in man.** Psychopharmacology. 62(2):129-132, 1979.

A partial evaluation is provided of whether the selective in vitro effects of clorgyline and pargyline might be demonstrable in vivo in man, both acutely and during the course of a 4 week drug administration period. During 4 weeks of treatment with clorgyline, platelet monoamine oxidase (MAO) activity was unchanged. During a similar 4 week crossover treatment period with pargyline, platelet MAO activity was essentially completely inhibited in the same individuals. The differential effects of the two drugs on platelet MAO, which consists exclusively of the MAO-B form suggests that the in vitro selectivity of clorgyline, and possibly of pargyline, on MAO-A and MAO-B may be maintained in vivo during long-term administration in man. Reductions in blood pressure, heartrate, and plasma amine oxidase activity were generally similar in magnitude during treatment with both drugs, however, suggesting that either these effects are nonspecific consequences of both MAO-A and MAO-B inhibition, or that pargyline also inhibited MAO-A activity. 25 references. (Author abstract modified)

004673 Narasimhachari, N.; Chang, S.; Davis, J. M. Dept. of Psychiatry, Medical College of Virginia, Richmond, VA 23298 **A test for antidepressant response to phenelzine.** Research Communications in Psychology, Psychiatry, and Behavior. 5(2):199-204, 1980.

A test for the acetylator status hypothesis for antidepressant response to phenelzine was examined. The lack of N-acetylphenelzine in plasma and urine samples of patients receiving 60mg phenelzine a day was determined using gas chromatographic mass spectrometric method. The levels of acetylated metabolite are extremely low and there is no difference between responders and nonresponders in plasma and urine levels of N-acetylphenelzine. It is concluded that acetylation is not a major metabolic pathway in phenelzine metabolism. 6 references. (Author abstract modified)

004674 Pond, Susan M.; Phillips, Michael; Benowitz, Neal L.; Galinsky, Raymond E.; Tong, Theodore G.; Becker, Charles E. Benowitz: 5H4 Clinical Pharmacology Unit, San Francisco General Hospital Medical Center, 1001 Potrero Avenue, San Francisco, CA 94110 **Diazepam kinetics in acute alcohol withdrawal.** Clinical Pharmacology and Therapeutics. 25(6):832-836, 1979.

Diazepam kinetics were studied in seven alcoholic subjects during acute alcohol withdrawal and after detoxification. The initial rapid exponential decline of plasma diazepam concentrations was more rapid during withdrawal than after detoxification. Terminal half-life, clearance, and volume of distribution changed in individual patients, but mean values did not change. Protein binding was lower in the patient group than in healthy controls. It is concluded that the effects of alcohol withdrawal on diazepam disposition do not explain the high doses of diazepam commonly required to treat the withdrawal. 10 references. (Author abstract modified)

004675 Potter, W. Z.; Calil, H. M.; Zavadil, A. P., III. Clinical Psychobiology Branch, NIMH, Bethesda, MD **Steady-state concentrations of hydroxylated metabolites of tricyclic antidepressants in patients: relationship to clinical effect.** Psychopharmacology Bulletin. 16(2):32-34, 1980.

The relationship to clinical effect of steady-state concentrations of hydroxylated metabolites of tricyclic antidepressants (imipramine and desipramine) were investigated in enuretic boys and adult depressed patients. The enuretic boys were treated with imipramine (IMI) or desipramine (DMI) in a double-blind cross-over protocol; adults were hospitalized major affective disorder patients and adult outpatients receiving chronic doses of IMI. Mean steady-state concentrations of IMI, 2-hydroxyimipramine (OH-IMI), DMI, and 2-hydroxydesipramine (OH-DMI), and ratios of these compounds were determined and evaluated. Since there is controversy concerning the relationship between plasma concentrations of tricyclic antidepressants and therapeutic efficacy, the finding that all active forms of drug have not been measured is clinically relevant. 9 references.

004676 Prange, Arthur J., Jr.; Loosen, Peter T.; Nemeroff, Charles B. Biological Sciences Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Peptides: application to research in nervous and mental disorders. (Unpublished paper).** Research Report, NIMH Grant MH-32316, 1979. 86 p.

An overview of peptides is presented which includes the behavioral and endocrine effects of hypothalamic hypophysiotropic hormones, anterior pituitary hormones, and opiate related substances. Thyrotropin releasing hormone effects on affective disorders, alcohol withdrawal syndrome, schizophrenia, and normal subjects are reviewed. The luteinizing hormone releasing hormone effects on affective disorders, alcoholism, schizophrenia, male sexual impotence, and normal subjects are presented. Melanocyte stimulating hormone releasing inhibiting factor in the treatment of affective disorders and Parkinson's disease, and somatotropin release inhibiting factor in Parkinson's disease, are reviewed. Also reviewed are: the effects of adrenocorticotropin hormone and related peptides in schizophrenia, hyperkinetic syndrome of children, convulsive disorders, and normal subjects; the effects of thyroid stimulating hormone in affective disorders; and the growth hormone. The posterior pituitary hormone vasopressin; the opiate related substances in depression, schizophrenia, pain states, and normal subjects; and the peptides insulin, glutathione, threonyl valyl leucine, cholecystokinin, and neurotension are reviewed. 303 references.

004677 Roberts, Roderick K.; Desmond, Paul V.; Wilkinson, Grant R.; Schenker, Steven. Schenker: V.A. Medical Center, 1310 24th Avenue South, Nashville, TN 37203 **Disposition of chlordiazepoxide: sex differences and effects of oral contraceptives.** Clinical Pharmacology and Therapeutics. 25(6):826-831, 1979.

The disposition of chlordiazepoxide was studied in 11 healthy young men, 11 healthy young women, and seven healthy young women who had been taking oral contraceptive (OC) steroids for more than 6 months. The elimination half-life was longer in women than in men, and protein binding was lower. Weight normalized plasma clearances of total drug did not differ, but clearance of unbound drug was significantly lower in women than in men. Women on OC steroids had a lower plasma binding and higher volume of distribution than women not on OC steroids. The elimination half-life was longer and clearance of unbound drug was lower in women on OC steroids than in those not using them, but these differences were not significant. 25 references. (Author abstract modified)

004678 Sannita, Walter G.; Rapallino, Maria V.; Rodriguez, Guido; Rosadini, Guido. Institute for Neurophysiopathology, University, Genoa, Italy **EEG effects and plasma concentrations of phenobarbital in volunteers.** Neuropharmacology. 19(9):927-930, 1980.

Parallel changes in plasma drug levels and EEGs were seen in five young women given a single oral dose of phenobarbital (100mg/m2 body surface). Plasma levels of phenobarbital were 2.1 to 7.6mcg/ml 1 hour after drug administration. Power spectral analysis revealed a consistent increase in the absolute power of EEG frequencies above 16 Hz, with the maximum effect 5 to 7 hours after drug administration. 10 references. (Author abstract modified)

004679 Schachter, M.; Bedard, P.; Debono, A. G.; Jenner, P.; Marsden, C. D. University Dept. of Neurology, King's College Hospital, London SE5 9RS, England **The role of D-1 and D-2 receptors.** Nature. 286(5769):157-159, 1980.

The role of D1 and D2 dopamine receptors in intracerebral motor and endocrine systems (D1 and D2 receptors differ only in the presence or absence of adenylate cyclase linkage, respectively) was investigated via pharmacological manipulations. A number of dopamine agonist and antagonist drugs that have different actions on D1 and D2 receptors in animals were investigated in Ss with Parkinson's disease, in which dopamine sensitive adenylate cyclase activity is reduced by at least 50%. Motor and endocrine effects in parkinsonian Ss seem to depend on drug interaction with D2, but not D1 receptors. These results are discussed in terms of their implications for the design of antiparkinsonian and antipsychotic agents. 30 references. (Author abstract modified)

004680 Schatz, F.; Jahn, U.; Wagner-Jauregg, Th.; Zirngibl, L.; Thiele, K. Sandox Forschungsinstitut, Vienna, Austria **1-Amino-3-phenylindoles with antidepressant activity: binodaline hydrochloride and related substances.** Arzneimittel Forschung. 30(6):919-923, 1980.

The synthesis of N-alkylated 1-amino-3-phenyl indoles, and especially the development of the antidepressant substance binodaline hydrochloride, is outlined. The ring structure of binodaline is compared to that of other antidepressant drugs with indole, indolenin, indazole, and benzimidazoline skeletons. The structure of the side chain is also compared to that of known tricyclic antidepressants. 21 references. (Author abstract modified)

004681 Sherman, Kathleen Anne. University of Pittsburgh **The effect of acute and chronic fluphenazine administration on cholinergic and dopaminergic mechanisms in rat striatum: dissertation).** Dissertation Abstracts International. 40(10):5068-B, 1980. Ann Arbor, Univ. Microfilms No. 8004877, 231p., 1979.

The effect of acute and chronic fluphenazine (FLU) administration on cholinergic and dopaminergic mechanisms in rat striatum was studied. The results suggest that after acute administration of neuroleptics such as FLU, the release and metabolism of acetylcholine (ACh) are enhanced but that a compensatory increase in choline (Ch) uptake (or ACh syntehsis) does not occur, and therefore a temporary decrease in ACh concentration results. This appears to reflect major differences in the regulation of ACh synthesis in striatum from that occurring in other brain regions. Chronic administration of FLU appeared to result in a net decrease in the ability of the drug to effectively antagonize the activation of the postsynaptic DA receptor adenylate cyclase complex by DA or DA agonists. This in turn may result in a restoration of the inhibitory influence of DA on striatal ACh release in the presence of the drug, and thus explain the tolerance to the effect of the neuroleptics on ACh content observed. Data on behavioral changes during chronic FLU administration suggest that striatal ACh containing interneurons may be involved in the regulation of food and water intake, but do not mediate the motor deficits induced by FLU in rats. (Journal abstract modified)

004682 Shore, David; Millson, Mark; Holtz, John; King, Steven; Savory, John; Wills, Michael; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Aluminum and parathormone in Alzheimer-type dementia. (Unpublished paper).** Washington, DC, NIMH, 1980. 2 p.

Serum parathyroid hormone (PTH) and serum aluminum concentrations were measured (PTH by radioimmunoassay and aluminum by flameless atomic absorption spectrophotometry) in 10 patients meeting DSM-III criteria for primary degenerative dementia (PDD). No significant elevations of serum PTH or serum aluminum were found in PDD patients. While aluminum may accumulate on CNS nuclear chromatin in such patients, this does not appear to be the result of a systematic overload of

aluminum or due to an excessive concentration of circulating PTH. It is suggested that failure research should focus on the mechanism of aluminum/DNA binding to discover whether such accumulations are reversible and whether they precede or follow neuronal degeneration in PDD. 3 references. (Author abstract modified)

004683 Smith, Robert C.; Misra, Chandra H.; Leelavathi, Doddamane E. Section of Behavioral Neurochemistry, Texas Research Institute of Mental Sciences, Houston, TX **Receptor studies of the effects and blood levels of neuroleptic and antidepressant drugs.** Psychopharmacology Bulletin. 16(3):84-85, 1980.

The use of receptor binding methods to study the relationship of blood levels to clinical effects of neuroleptics and antidepressant drugs in man, and also the interaction of age and treatment and chronic administration of neuroleptic drugs in the rat is described. A chemical assay for plasma nortriptyline and haloperidol (gas liquid chromatography with a nitrogen detector; GLC) levels was compared with receptor binding assays for the evaluation of blood levels and clinical effects. In comparison to nortriptyline, haloperidol blood levels obtained by the two methods had a much higher correlation in most patients. However, for both drugs, there were important patient differences.

004684 Syvalahti, E.,; Nagy, A.; van Praag, H. M. Medical Dept., Astra Lakemedel AB, S-151 85 Sodertalje, Sweden **Effects of zimelidine, a selective 5-HT uptake inhibitor, on serum prolactin levels in man.** Psychopharmacology. 64(3):251-253, 1979.

The levels of serum prolactin were studied in humans both after an acute intake of zimelidine and during a treatment period of 3 to 7 weeks. No significant changes in basal serum prolactin levels were seen after single oral doses of zimelidine (100mg) in healthy volunteers during an investigation period of 12 hours. Serum prolactin concentrations remained well within the pretreatment levels also during a continuous treatment of depressive patients with zimelidine up to 150mg orally b.i.d. It is concluded that clinical doses of the selective 5-hydroxytryptamine uptake inhibitor zimelidine does not exert any significant effect on serum prolactin level. 17 references. (Author abstract modified)

004685 Troupin, Allan S.; Friel, Patrick; Lovely, Mary Pat; Wilensky, Alan J. Dept. of Neurology, Hospital of the University of Pennsylvania, 34th and Spruce Sts., Philadelphia, PA 19104 **Clinical pharmacology of mephenytoin and ethotoin.** Annals of Neurology. 6(5):410-414, 1979.

Single dose studies of mephenytoin and ethotoin were performed in adult inpatients on stable regimens of other anticonvulsants. Following oral administration of 7mg/kg mephenytoin, peak serum concentrations were achieved in 1 hour; the drug had a half-life of 7 hours, compared to 96 hours for its metabolite, 5-ethyl-5-phenylhydantoin. After oral administration of 25mg/kg ethotoin, peak serum concentration was achieved in 2 hours, with a drug half-life of 5 hours. Saliva accurately represented the unbound fraction for all three agents; mean salivary levels were 61% for mephenytoin, 73% for its metabolite, and 54% for ethotoin. It is concluded that the short half-life of ethotoin would require divided daily doses to achieve steady-state. After mephenytoin administration, stable blood levels of its metabolite and anticonvulsant effectiveness can be achieved on simple dose schedules. 11 references. (Author abstract modified)

004686 Tuomisto, Jouko; Tukiainen, Erkki; Voutilainen, Raija; Tuomainen, Paivi. University of Kuopio, P.O.B. 138, SF-70101 Kuopio 10, Finland **Inhibition of 5-hydroxytryptamine and noradrenaline uptake in platelets and synaptosomes incubated in plasma from human subjects treated with amitriptyline or nortriptyline: utilization of the principle for a bioassay method.** Psychopharmacology. 69(2):137-142, 1980.

To estimate the inhibition of amine uptake caused in vivo by tricyclic drugs used at a clinical dose, normal human blood platelets or rat hypothalamic or cortical synaptosomes were incubated with (3H)5-hydroxytryptamine ((3H)5-HT) or (3H)noradrenaline ((3H)NA) in platelet free plasma of healthy volunteers receiving a single dose of 50mg amitriptyline (AT) or nortriptyline (NT) orally. Venous blood samples were taken 2 to 72 h after drug administration. AT and NT were assayed via gas chromatography. In most experiments there was a correlation between the gas chromatographically assayed AT or NT and uptake inhibition. 5-HT uptake in platelets were inhibited by both drugs and so was NA uptake in rat cortical synaptosomes. 5-HT uptake by hypothalamic synaptosomes, however, was not sensitive enough to reveal the small concentrations of drugs. In platelets, a poor correlation was found 12 h post AT administration, since the effect found in the biological assay outlasted the chemically assayed AT and NT. Tricyclic antidepressants are metabolized to a variable degree to both active and inactive metabolites. 17 references. (Author abstract modified)

004687 Vallner, J. J.; Kotzan, J. A.; Stewart, J. T.; Honigberg, I. L.; Needham, T. E.; Brown, W. J. Biological Availability Group, School of Pharmacy, University of Georgia, Athens, GA 30602 **Plasma levels of clobazam after 10-, 20-, 40-mg tablet doses in healthy subjects.** Journal of Clinical Pharmacology. 20(7):444-451, 1980.

Substantial intersubject and intrasubject variability in bioavailability of clobazam was observed after ingestion of 10, 20, and 40mg tablets by healthy volunteers. Peak concentrations and area under the plasma level/time curve were directly proportional to dose. Mean plasma half-life was about 18 hours, which compares favorably with the half-life of other benzodiazepines. 9 references.

004688 Viswanathan, C. T.; Booker, Harold E.; Welling, Peter G. Welling: School of Pharmacy, University of Wisconsin, Madison, WI 53706 **Pharmacokinetics of phenobarbital following single and repeated doses.** Journal of Clinical Pharmacology. 19(5-6):282-289, 1979.

Serum levels of phenobarbital and urinary excretion of phenobarbital and p-hydroxyphenobarbital were determined after single and repeated 30mg oral doses in three healthy male volunteers. The serum levels of phenobarbital at steady state were about 10 times higher than those seen after a single dose. Five day urinary excretion of phenobarbital and p-hydroxyphenobarbital accounted for 16 and 21% respectively of the initial dose. Comparison of plasma and renal clearances indicated that the rate of phenobarbital metabolism was reduced with repeated dosing, while the rate of urinary excretion of the parent drug was unchanged. 8 references.

004689 Vogelzang, Nicholas J.; Frenning, Daniel H. University of Minnesota, Minneapolis, MN 55455 **Lithium and hematopoiesis.** New England Journal of Medicine. 303(9):525, 1980.

A case history is reported of a 63-year-old woman with severe marrow hypoplasia induced by chemotherapy and radiation, who was treated with lithium carbonate. The lithium had a short-term effect. The patient required no further transfusions and the ecchymoses and epistaxis stopped. The rapid recurrence of symptoms after a 4 month interval suggests that lithium stimulation of the stem cells had ceased.

004690 Volavka, Jan; James, Barbara; Reker, D.; Mallya, A.; Cho, D.; Pevnick, J. Missouri Institute of Psychiatry, 5400 Arsenal Street, St. Louis, MO 63139 **EEG and other effects of nal-**

trexone and heroin in man. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):79-85, 1979.

Previously reported data on EEG and behavioral effects of heroin and opiate antagonists in exaddicts are reviewed, and new findings on the effects of naltrexone in men who have never been addicted are presented. Ten normal volunteer Ss were given on three separate occasions, placebo, 50mg or 100mg of naltrexone. The average alpha frequency was significantly slower after naltrexone than after placebo. Naltrexone elicited a significant reduction of breathing rate and oral temperature. Results indicate that naltrexone does not act as a pure narcotic antagonist in nonaddicted men. 25 references. (Author abstract modified)

004691 Wiesel, F. -A.; Alfredsson, G.; Ehrnebo, M.; Sedvall, G. Laboratory of Experimental Psychiatry, Dept. of Psychiatry, Karolinska Hospital, S-1041 Stockholm 60, Sweden **The pharmacokinetics of intravenous and oral sulpiride in healthy human subjects.** European Journal of Clinical Pharmacology. 17(5):385-391, 1980.

The pharmacokinetics of sulpiride was studied in six healthy volunteers after intravenous and oral (tablets) administration of 100mg sulpiride. An open two compartment or three compartment (two Ss) model was applied following intravenous administration. The average total distribution volume during the terminal slope was 2.72 or - 0.661/kg and total systemic clearance was 415 or - 84ml/min. The serum half-life on the terminal slope following intravenous administration averaged 5.3. h according to the two compartment model. In two Ss the half-lives were 11.0 and 13.9 h when the three compartment model was applied. Determination of urinary excretion rates of unchanged sulpiride indicated a half-life of 7.15 h. Following intravenous administration, 70% of the dose was recovered unchanged in urine within 36 h; the mean renal clearance was 310 or - 91ml/min. Sulpiride was absorbed slowly, with peak concentrations appearing between 3 and 6 h after oral administration. The recovery of unchanged drug in urine following oral administration was 15% of the dose, with a mean renal clearance of 233 or - 47ml/min. The bioavailability determined from combined plasma and urine data was only 27%. The low bioavailability was probably due to incomplete absorption. 13 references. (Author abstract modified)

004692 Young, Robert J.; Lawson, A. A. H.; Malone, D. N. S. Diabetic Dept., Royal Infirmary, Edinburgh, Scotland **Treatment of severe hypertension with chlorpromazine and frusemide.** British Medical Journal. 280(6231):1579, 1980.

A prospective study of the use of chlorpromazine and frusemide in the treatment of nine cases of severe hypertension is described. Chlorpromazine is a major tranquillizer with a complex action on the cardiovascular system resulting in hypotension. Frusemide, a loop diuretic, has an initial acute volume depleting effect on the circulation. A gradual and adequate reduction in blood pressure and pulse rate resulted in each of the nine cases. The method is simple to administer; the rate of action is gradual and predictable, without reflex tachycardia; and is not contraindicated in cardiac failure or asthma. In this series, the maximum fall in mean arterial pressure was considerably less than that at which cerebral hypoperfusion has been shown to lead to cerebral ischemia and risk of permanent neurological deficit. 4 references.

004693 Zilm, D. H. Human Responses and Biomedical Engineering Laboratory, Addiction Research Foundation, 33 Russell St., Toronto, Canada M5S 2S1 **Naloxone response in non-dependent man: effect on six physiological variables.** Neuropharmacology. 19(7):591-595, 1980.

Six physiologic responses were measured in normal nonaddicted male Ss given i.v. infusions of 1.2mg naloxone or saline. Naloxone produced a slight miosis, increased rate of core temperature drop, and reduced blood pressure. Heartrate, respiratory rate, and hand tremor did not differ significantly after the two treatments. Results suggest that naloxone may possess slight opiate agonist properties or interact with endogenous opiate substances. 22 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

004694 Bassi, S.; Albizzati, M. G.; Frattola, L.; Passerini, D.; Trabucchi, M. Dept. of Neurology, Pad. Ponti-Policlinico, Via F. Sforza 35, I-20122 Milan, Italy **Dopamine receptors and sleep induction in man.** Journal of Neurology, Neurosurgery and Psychiatry. 42(5):458-460, 1979.

Sleep induction was studied in humans after the administration of apomorphine, a direct stimulant of the central dopaminergic system. The drug induced sleep and vomiting in healthy volunteers while it had no significant effect on 10 Parkinsonism patients treated for a long period with L-dopa. Apomorphine given to a group of Parkinsonism patients not receving any specific treatment, and with a lower degree of disease severity, induced vomiting and sleep with a pattern similar to that in healthy subjects. A relationship between the dopaminergic system and sleep induction is suggested. 14 references. (Author abstract)

004695 Beal, Don; Dujovne, Carlos; Gillis, John S. Dept. of Psychology, Miami University, Oxford, OH 45056 **The effect of methyldopa on human judgment in hypertensive patients and normal volunteers.** Research Communications in Psychology, Psychiatry, and Behavior. 5(2):205-217, 1980.

The acute effects of methyldopa on judgmental learning in groups of hypertensive patients and normal subjects were examined. Using a judgmental learning task it was found that during the acute phase the drug was associated with impairment in human judgment in the volunteers, but not in the hypertensive patients. It appears that methyldopa does affect certain parameters of cognitive functioning in its early use. 15 references. (Author abstract modified)

004696 Belgrave, B. E.; Bird, K. D.; Chesher, G. B.; Jackson, D. M.; Lubbe, K. E.; Starmer, G. A.; Teo, R. K. C. Jackson: Dept. of Pharmacology, University of Sydney, Sydney, New South Wales 2006, Australia **The effect of cannabidiol, alone and in combination with ethanol, on human performance.** Psychopharmacology. 64(2):243-246, 1979.

The effects of cannabidiol (CBD, 320microgram/kg) or placebo followed by comsumption of an ethanolic beverage (.54g/kg) or placebo 60 min later on performance were investigated in 15 volunteers. Effects were measured 100 min, 160 min, and 220 min after CBD ingestion using cognitive, perceptual, and motor function tests. Factorial analysis indicated that test procedures could be adequately expressed by three rotated factors: a reaction speed factor (I); a standing steadiness factor (I), and a psychomotor coordination/cognitive factor (III). Ethanol produced a significant decrement in factor III. There was no demonstrable effect of CBD, either alone or in combination with ethanol. Neither ethanol nor CBD produced any significant effect on pulse rate. Prior administration of CBD did not significantly affect the blood ethanol levels. While the subjects were able to identify correctly when they were given ethanol, they did not report any subjective effects of CBD. 19 references. (Author abstract modified)

004697 Belmore, Susan M.; Miller, Loren L. Miller: Burroughs Wellcome Co., Research Triangle Park, NC **Levels of processing**

and acute effects of marijuana on memory. Pharmacology Biochemistry and Behavior. 13(2):199-203, 1980.

Male volunteers' memory for lists of words was tested after each S smoked a single marijuana cigarette containing 1.4% delta9-tetrahydrocannabinol or a placebo cigarette. When intoxicated with marijuana, Ss recalled fewer words and were more likely to forget meaningfully processed words on recently presented lists. However, no differential drug effects on processing and retention of different types of linguistic information (orthographic, phonetic, semantic, or syntactic) were demonstrated. 20 references. (Author abstract modified)

004698 Berrhyill, Richard E.; Benumof, Jonathan L.; Janowsky, David S. Benumof: Dept. of Anesthesia Research Laboratory, M-004, University of California, San Diego, La Jolla, CA 92093 **Morphine-induced hyperexcitability in man.** Anesthesiology. 50(1):65-66, 1979.

A case history of a 72-year-old man who experienced a dramatic stimulatory effect (hyperexcitability) following intravenous administration of morphine during the induction of anesthesia is reported. The case is important for two reasons. First, it documents the occurrence of a stimulatory effect of morphine in man, and, although the mechanism underlying this phenomenon is speculative, its occurrence may serve as a link, relating animal data to human physiology. Second, and of more practical importance, the description of morphine induced hyperactivity in man alerts physicians to a new, possibly adverse reaction to morphine. 15 references.

004699 Bowerman, W. Maurice. 4350 S. W. Cedar Hills Blvd., Beaverton, OR 97005 **Paradoxical effects of Ritalin in adults.** Journal of Orthomolecular Psychiatry. 9(3):223-227, 1980.

Two conditions among adults which are probably related to minimal brain dysfunction are described, and the responses of these adults to methylphenidate (Ritalin) are discussed. Both acutely paranoid prisoners and another group of inmates whose complaints were more neurotic in terms of fatigue, lassitude, hypochondrical preoccupations demonstrated the same paradoxical, normalizing response to Ritalin, and abnormal glucose metabolism. It is concluded that many of the men in this penitentiary were diagnosable as having minimal brain dysfunction (and had manifested substantial learning problems in school), that they reacted in the same paradoxical or normalizing way to Ritalin, and that many of these same patients also responded to low carbohydrate diets, multiple feedings during the day and additional vitamins. 3 references.

004700 Brady, John Paul; Bianco, C. Fernando. Hospital of the University of Pennsylvania, Philadelphia, PA 19104 **Endorphins: naloxone failure to increase sexual arousal in sexually unresponsive women: a preliminary report.** Biological Psychiatry. 15(4):627-631, 1980.

Three physically normal and healthy women, but with histories of low sexual arousability, were administered naloxone or saline in a double-blind study in order to determine whether naloxone can increase sexual arousal. No subject showed evidence that naloxone could enhance sexual arousal to erotic stimuli. 13 references.

004701 Breier, Christoph; Kain, Herbert; Konzett, Heribert. Dept. of Pharmacology, University of Innsbruck, Peter-Mayr-Strasse 1, A-6020 Innsbruck, Austria **Personality dependent effects of the ACTH 4-10 fragment on test performances and on concomitant autonomic reactions.** Psychopharmacology. 65(3):239-245, 1979.

The effect of the ACTH fragment 4-10 on a mental performance test and on some concomitant cardiovascular changes was investigated. The subjects were either mainly extraverted or mainly introverted according to Eysenck's Maudsley Personality Inventory. Under the influence of the heptapeptide, extraverted subjects achieved a higher total score in the mental task performance with a smaller increase of forearm blood flow and of heartrate than under the influence of the placebo. In contrast, under the influence of the placebo, introverted subjects achieved a higher total score in the mental task performance with a smaller increase of physiological changes under the influece of the ACTH fragment. Personality, therefore, determines to some degree how this centrally acting heptapeptide influences efficiency in the mental task performance. 18 references. (Author abstract)

004702 Brena, Steven F.; Wolf, Steven L.; Chapman, Stanley L.; Hammonds, William D. Dept. of Rehabilitation Medicine, Pain Control Center, Emory University, Atlanta, GA 30322 **Chronic back pain: electromyographic, motion and behavioral assessments following sympathetic nerve blocks and placebos.** Pain. 8(1):1-10, 1980.

The effects of 12 lumbar sympathetic injections (in a series of six with bupivacaine and six with saline, sympathetic nerve block and placebo conditions, respectively) on subjective pain intensity, EMG from paravertebral muscles, joint ranges of mobility on 20 chronic low back pain patients were assessed throughout treatment and at 3 month followup. MMPI profiles were also assessed pretreatment, posttreatment, and at 3 month followup. Results reveal significant reductions in subjective pain intensity lasting 1 month after treatment which were not significantly different during bupivacaine and saline injection periods. Patients' MMPI profiles were indicative of reduced depression and an increase in ability to manage their lives. No significant changes were recorded with respect to EMG, joint range mobility, or daily activity levels. Results are discussed in terms of massive placebo effect and analgesia obtained through hyperstimulation of various tissue structures, and are consistent with the hypothesis that central postsynaptic mechanisms were predominant in these patients' pain states. Because subjective pain decrease did not independently produce increased functioning, deep analgesic injections or other pain relieving techniques matched with behavior modification is recommended for functional rehabilitation. 16 references. (Author abstract modified)

004703 Carrol, Edward Nicholas. University of Delaware **A test of the optimal level of arousal theory of sensation seeking. (Ph.D. dissertation).** Dissertation Abstracts International. 40(4):1882-B, 1979. Ann Arbor, Univ. Microfilms No. 7921824, 154p., 1979.

The theoretical assumption that high sensation seekers (HSSs) feel and function better than low sensation seekers (LSSs) under conditions of heightened arousal while, conversely, lows perform better than highs when central nervous system arousal levels are dampened was tested. Thirty two medical students who scored in either the top or bottom deciles of their class on the total raw score of the Sensation Seeking Scale were administered, double-blind, either calcium carbonate (placebo), dextroamphetamine sulfate (stimulant), diazepam or (depressant), one drug at each session. Despite the effectiveness of the drugs in producing highly significant differences in effect from one another in the total sample, multivariate statistics indicated that HSSs and LSSs did not respond differentially to any of the three experimental conditions. Responses were not consistent with an optimal level of arousal model of sensation seeking. (Journal abstract modified)

004704 Crayton, John W. University of Chicago, Dept. of Psychiatry, 950 East 59th St., Chicago, IL 60637 **The effect of dia-**

zepam on the spinal monosynaptic (H-) reflex in man. Neuropharmacology. 19(9):915-918, 1980.

To determine the effect of diazepam on the excitability of alpha-motoneurons, the recovery curve of the H-reflex was measured in 12 Ss after oral doses of 10 or 20mg diazepam. Diazepam significantly reduced the peak of secondary facilitation; this effect was maximal 1 hour after the low dose and 2 hours after the higher dose. No significant changes in other H-reflex parameters were noted. Results are consistent with the suggestion that diazepam acts primarily on supraspinal mechanisms with descending influences on spinal motoneuron excitability. 7 references. (Author abstract modified)

004705 Crowley, Thomas J.; Hydinger-Macdonald, Marilyn. Dept. of Psychiatry, University of Colorado, Medical Center, Denver, CO 80262 **Bedtime flurazepam and the human circadian rhythm of spontaneous motility.** Psychopharmacology. 62(2):157-161, 1979.

For 24 hr after each treatment with either bedtime placebo or flurazepam, the spontaneous motor activity of 16 male students was recorded each 15 min with an unobtrusive actometer, worn as the subjects attended classes. Althought the drug did not consistently modify reports of subjective feelings on the Profile of Mood States (POMS), 13 subjects correctly discriminated drug from placebo sessions. A bedtime dose of 30mg of flurazepam significantly reduced spontaneous human motility that night and during the next day. Activity recording revealed an important residual, behavioral effect of the drug which was not reflected in POMS reports of subjective feelings, suggesting that activity recording may provide a more sensitive measure for psychotropic drug effects. 19 references. (Author abstract modified)

004706 Delwaide, P. J.; Hurlet, A. Institut de Medicine, Hopital de Baviere, Bd de la Constitution 66, B-4020 Liege, Belgium **Bromocriptine and buccolinguofacial dyskinesias in patients with senile dementia: a quantitative study.** Archives of Neurology. 37(7):441-443, 1980.

Eight women with senile dementia and buccolinguofacial dyskinesias (BLFD) were given bromocriptine mesylate. The frequency of their abnormal movements was quantified by repeated counts (220 per patient). In six patients, the mean frequency of BLFD was lower during bromocriptine mesylate therapy as compared with placebo; this result was statistically significant in four of the six. The second day after cessation of bromocriptine therapy, there seemed to be a rebound effect in six patients. These phenomena are discussed in light of the possible existence of presynaptic autoreceptors that would explain the paradoxical effects produced by a number of dopamine agonists. 19 references. (Author abstract)

004707 Farhoumand, N.; Harrison, J.; Pare, C. M. B.; Turner, P.; Wynn, S. Dept. of Psychological Medicine, St. Bartholomew's Hospital, London, EC1, England **The effect of high dose oxprenolol on stress-induced physical and psychophysiological variables.** Psychopharmacology. 64(3):365-369, 1979.

The effects of high dose, oral oxprenolol (480mg) and lorazepam (2mg) on stress induced physical and psychophysiological variables (skin conductance, reaction time, critical flicker frequency, and self-rating visual analogue scales for anxiety, sedation, and concentration) were investigated in six healthy male volunteers. Oxprenolol exerted a central action similar to lorazepam as shown by a significant lowering of skin conductance and decrease in the number of spontaneous fluctuations during stress, impaired critical flicker frequency, and decrease in alertness with reduced concentrations. It is noted that this is the first controlled experimental study in which a beta-adrenoceptor blocking drug used in high dose has been shown to influence tests of CNS function in man. 21 references. (Author abstract modified)

004708 Fink, M.; Irwin, P. State University of New York at Stony Brook, Dept. of Psychiatry and Behavioral Science, Stony Brook, NY 11794 **CNS effects of the antihistamines diphenhydramine and terfenadine (RMI 9918).** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(1):35-44, 1979.

The quantitative EEG profile of a putative antihistaminic drug, terfenadine (RMI 9918), was determined in a crossover comparison with diphenhydramine in normal male volunteers. Terfenadine failed to elicit the characteristic EEG or behavioral effects of sedative antihistaminics, and was distinguishable from diphenhydramine. The EEG profile confirmed the lack of CNS effect observed in preclinical and clinical trials. 25 references. (Author abstract)

004709 Fischman, Marian W.; Schuster, Charles R. Dept. of Psychiatry, Pritzker School of Medicine, University of Chicago, 950 East 59th Street, Chicago, IL 60637 **The effects of chlorpromazine and pentobarbital on behavior maintained by electric shock or point loss avoidance in humans.** Psychopharmacology. 66(1):3-11, 1979.

The effects of pentobarbital and chlorpromazine on human escape and avoidance behavior motivated by electric shock or token loss were investigated. Human volunteer Ss were trained to press a lever to avoid or escape electric shock of loss of points which could be redeemed for money. Both aversive stimuli maintained behavior which was differentially sensitive to these two drugs. Chlorpromazine caused a decrease in avoidance responding at doses which had little effect on escape responding. Pentobarbital, in contrast, suppressed avoidance responding at doses which also had a suppressant effect on escape responding. 20 references. (Author abstract modified)

004710 Gifford, Susan Dalton. North Texas State University **A comparison of drug treatment for insomnia and the effect of causal attribution. (Ph.D. dissertation).** Dissertation Abstracts International. 40(3):1365-B, 1979. Ann Arbor, Univ. Microfilms No. 7919722, 59p., 1979.

A double-blind comparison was conducted for treatment of insomnia using secobarbital, flurazepam hydrochloride, and thioridazine, and a placebo. Half of the subjects in each of the four groups were told if the drug had caused any observed changes in their sleep behavior, and the other half were told the drugs were not typically used to treat insomnia and changes in their sleep were due to changes made in their sleep behavior internally. Results indicate that there were reductions in latency with no significant differences among any of the groups. Additionally, the decreases in latency were maintained regardless of the subjects' attributions about why the change occurred. Reduction in latency to sleep was significantly greater during drug administration than pretreatment or posttreatment periods and the reduction was maintained during posttreatment as compared to preexperimental levels. The implications for clinicians is that a short course of drug therapy using a placebo or one of several soporific drugs might be used equally effectively to treat primary latency insomnia. (Journal abstract modified)

004711 Gruzelier, John; Thornton, Susan; Staniforth, David; Zaki, Saniha; Yorkston, Neil. Dept. of Psychiatry, Charing Cross Hospital Medical School, Fulham Palace Road, London W6 8RF, England **Active and passive avoidance learning in controls and schizophrenic patients on racemic propranolol and neuroleptics.** British Journal of Psychiatry. 137(August):131-137, 1980.

The effect of propranolol on active and passive/avoidance learning was investigated with 17 schizophrenics and 13 normal controls. Controls and schizophrenics on propranolol as sole drug or combined with neuroleptics showed superior active and passive/avoidance learning, as compared to schizophrenics medicated with conventional neuroleptics only. Active avoidance involved responding quickly, passive/avoidance withholding a response to avoid an unpleasant noise and reacting to the appropriate stimulus. These results may reflect an improvement brought about by propranolol in the limbic regulation of stimulus and response processes. 25 references. (Author abstract modified)

004712 Hartley, Laurence. Dept. of Psychology, Murdoch University, Murdoch 6153, Western Australia, Australia **Diazepam: human learning of different materials.** Progress in Neuro-Psychopharmacology. 4(2):193-197, 1980.

The effects of diazepam on human learning was investigated in two small scale experiments with normal Ss in a state dependent learning paradigm. Results indicate that a low dose of 5mg of diazepam during learning and present in the body after learning can facilitate later recall, and that this effect is not state dependent. Furthermore, there is some evidence that the recall of material is changed by the presence of the drug; recall of words as compared to pictures was improved by drug administration during recall, independently of drug administration or nonadministration during learning. Improved sleep during the intervening night is discussed as a possible explanation for these effects. 7 references. (Author abstract modified)

004713 Jenkins, J. S.; Mather, H. M.; Coughlan, A. K.; Jenkins, D. G. Dept. of Medicine, St. George's Hospital Medical School, London SW17 0RE, England **Desmopressin in post-traumatic amnesia.** Lancet. No. 8154:1245-1246, 1979.

The effect of desmopressin on memory impairment arising from severe head injuries were studied. Six male Ss ages 24 to 36 years old were injured in traffic accidents 3 to 8 years previously. Their periods of unconsciousness had ranged from 5 weeks to 3 months. A series of psychometric tests of memory and intellect were carried out at the beginning of the study, and desmopressin (DDAVP) was administered intramuscularly in a dosage of 4microg daily for 5 weeks. The tests used were: Raven's progressive matrices, digit span forward, digit span backward, the Benton visual retention test (administration A), forced-choice word recognition, cued word recall, and yes/no word recognition. When IQs derived from reading abilities were compared with those derived from matrices' scores, five of the six showed evidence of intellectual impairment, and all six showed evidence of memory impairment. There were no significant differences between performances, except on digit span backward, when performances on DDAVP were significantly worse than those preceding or following it. EEGs conducted before and at the end of treatment indicated no changes in the pattern. The patients were subsequently given lysine-vasopressin intranasally four times daily for 6 weeks, but again no significant changes in memory were found. It is suggested that higher doses or active analogues with a better penetration into the brain may be required. 8 references.

004714 Kohnen, R.; Lienert, G. A.; Schmidt, F. I. Fachbereich Erziehungs- und Kulturwissenschaften, Universitat Erlangen-Nurnberg, Regensburger Strasse 160, D-8500 Nuremberg, Germany **/Clinicophysiological sleep and hangover spectra from pentobarbital, promazin and their combination, as reflected by self-ratings of young and elderly subjects./** Klinisch-psychologische Schlaf- und Nachwirkungspektren von Pentobarbital, Promazin und ihrer Kombination im Spiegel der Selbstbeurteilung junger und alter Versuchspersonen. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(3):261-268, 1979.

To determine whether and how promazine interacts with pentobarbitol as a hypnotic agent, eight young and eight elderly subjects were examined in a 2 x 2 x 2 factorial design. Results from self-reports concluded that: 1) young subjects did not experience any significant effects from either the single components and/or their combination; and 2) elderly subjects experienced positive effects in sleep and hangover parameters under the single components, as well as under the combination. Consequences for research in clinical psychopharmacology are discussed. 10 references. (Journal abstract modified)

004715 La Selva, V.; Nava, D. Ospedale Geriatrico Opera Pia Italy **/Preliminary note on the utilization of etoperidone in the treatment of the disturbance of chronic cerebrovascular insufficiency: double-blind comparison with Hydergine./** Nota preliminare sull'impiego dell'etoperidone nel trattamento dei disturbi da insufficienza vascolocerebrale cronica: confronto in doppiocieco con diidroergotossina. Rivista di Neuropsichiatria e Scienze Affini. 25(2):57-68, 1979.

The utilization of a new psychotropic drug, etoperidone, versus the traditional Hydergina in the treatment of chronic cerebrovascular insufficiency was investigated in a double-blind study. The sample consisted of 16 elderly women suffering from various cerebral disturbances. The subjects were administered 50mg of etoperidone and 1.5mg of diidroergotossine in capsule form daily; the treatment lasted 30 days. Results indicate that the new psychotropic drug exerts good efficacy, at least equal to that exerted by Hydergina, and is statistically superior with regard to reestablishing mood tone, sociability and cooperation in the treated subjects. 8 references. (Journal abstract modified)

004716 Liljequist, Raija; Mattila, M. J. Dept. of Pharmacology, University of Helsinki, Helsinki 17, Finland **Acute effects of temazepam and nitrazepam on psychomotor skills.** Acta Pharmacologica et Toxicologica. 44(5):364-369, 1979.

The effects of temazepam and nitrazepam on short-term memory, paired association learning, reactive and coordinative skills, and critical flicker fusion were determined in 12 healthy volunteers. Nitrazepam (10mg) increased reaction and coordination errors and impaired learning and memory. A 10mg dose of temazepam impaired coordinative skills, and a 20mg dose impaired coordination, learning, and memory. Both drugs induced subjective sedative effects. All drug effects were most pronounced during the first 3 hours, but nitrazepam impaired learning even 8 hours after drug administration. 18 references. (Author abstract modified)

004717 Mendelson, Wallace B.; Slater, Stanley; Gold, Philip; Gillin, J. Christian. Biological Psychiatry Branch, Building 10, Rm 3N224, NIMH, 9000 Rockville Pike, Bethesda, MD 20205 **The effect of growth hormone administration on human sleep: a dose-response study.** Biological Psychiatry. 15(4):613-618, 1980.

The effects of growth hormone administration on sleep, learning, and affect in normal human subjects were examined. Human growth hormone and saline were administered for one night each to volunteers in a cross-over study. A dose of two units i.m. given 15 min before bedtime had no effect on sleep EEG parameters. In contrast five units resulted in a 19% decrease in slow wave sleep and a 13% increase in REM sleep. Neither dose, when given during daytime, affected tests of affect or serial learning. 14 references. (Author abstract)

004718 Parker, E. S.; Birnbaum, I. M.; Weingartner, H.; Hartley, J. T.; Stillman, R. C.; Wyatt, R. J. LLP-NIMH, Bldg. 31,

NIH, Bethesda, MD 20205 **Retrograde enhancement of human memory with alcohol.** Psychopharmacology. 69(2):219-222, 1980.

In two experiments with normal male Ss, the ingestion of alcohol (1ml/kg) immediately after learning significantly improved subsequent remembering. By comparison, marijuana (15mg) had no significant postacquisition effect. Facilitation of visual and verbal memory with alcohol under these conditions has implications for the interference and consolidation views of memory. These results also illustrated the importance of considering the effects of a drug on different stages of memory, since the same dose of alcohol impairs human memory when administered before learning, facilitates memory when administered shortly after acquisition, and has no effect when administered at the time of retrieval. 32 references. (Author abstract modified)

004719 Petersen, Ronald C. Mayo Medical School, Rochester, MN 55901 **Scopolamine state-dependent memory processes in man.** Psychopharmacology. 64(3):309-314, 1979.

Scopolamine state-dependent learning was investigated in humans using four learning and recall tasks. Twenty eight Ss performed the four tasks on the first day of the 2 day experiment under either the influence of the drug (mcg/kg of scopolamine i.v.) or a placebo and tried to recall the material on the second day in either the same or altered drug state. State-dependent learning throry predicts that those Ss in the same drug state on both days should recall more material than those who had their drug condition changed. Results confirmed this prediction for the two recall tasks which did not involve recall cues or prompts but not for the tasks involving memory aides. This implies that the drug state has memory cueing properties of its own and that recall can be enhanced either by restoring the drug state which existed at the time of learning or by providing external prompts. 20 references. (Author abstract)

004720 Petersen, Ronald C.; Ghoneim, Mohamed M. Ghoneim: Dept. of Anesthesia, University of Iowa Hospitals, Iowa City, IA 52242 **Diazepam and human memory: influence on acquisition, retrieval, and state-dependent learning.** Progress in Neuro-Psychopharmacology. 4(1):81-89, 1980.

The effects of diazepam on learning and memory processes in humans were evaluated using five tasks involving free and cued recall and mental imagery. State-dependent learning was assessed by manipulating the drug condition (diazepam or placebo) during the learning and recall sessions. Results indicate that 0.3mg/kg diazepam administered orally significantly impairs Ss' ability to learn new material using a variety of procedures. Retrieval of material once learned is not severely impaired by the drug. Although some evidence for state-dependent learning was found, additional studies are urged. 16 references. (Author abstract modified)

004721 Pfefferbaum, Adolf; Davis, Kenneth L.; Coulter, Cynthia L.; Mohs, Richard C.; Tinklenberg, Jared R.; Kopell, Bert S. Psychiatry Service, 116A3, VA Hospital, Palo Alto, CA 94304 **EEG effects of physostigmine and choline chloride in humans.** Psychopharmacology. 62(3) 225-233, 1979.

The EEG effects of physostigmine and choline chloride in 17 normal volunteers were examined in a plaebo/drug/placebo single-blind design. Eleven healthy elderly volunteers with mild memory impairment were treated with placebo followed by oral choline chloride. The larger doses of physostigmine produced an increase in low frequency activity and a slowing of the peak alpha frequency. Oral choline chloride had no effect on the EEG as measured by spectral analysis, but appeared to have differential effects on contingent negative variation (CNV) amplitude and reaction time, depending upon the initial CNV amplitude. 27 references. (Author abstract modified)

004722 Preskorn, Sheldon H.; Schwin, Robert L.; McKnelly, William V. Schwin: Veterans Administration Medical Center, 4801 Linwood Boulevard, Kansas City, MO 64128 **Analgesic abuse and the barbiturate abstinence syndrome.** Journal of the American Medical Association. 244(4):369-370, 1980.

Two cases of abstinence syndrome secondary to withdrawal from a combination analgesic containing 200mg aspirin, 40mg caffeine, 130mg phenacetin, and 150mg of butalbital (a short to intermediate acting barbiturate) are reported. In the first case, a 68-year-old woman was admitted with presenting symptoms including confusion and disorientation as to person, place, and time, labile and euphoric mood, pressure of speech and tangential thinking, auditory hallucinations, and grandiose delusions. In this case the patient had been taking doses of barbiturate equal to more than 1500mg/day for 6 to 12 months; symptoms appeared after a family member had hidden the prescription drug from the patient. In the second case, a 59-year-old-male had also been taking a barbiturate dose of over 1500mg/day. On admission to the hospital for chronic headache, all medication was withdrawn. Within 3 days, the patient became agitated, confused and disoriented, insomniac, tremulous, and complained of auditory hallucinations. In both cases, psychiatric consultation was necessary before proper therapy was initiated: the admitting physicians in both cases thought the complaints attributable to a functional psychiatric disorder rather than an acute organic brain syndrome. 6 references. (Author abstract modified)

004723 Reid, William H.; Gutnik, Bruce D. N.P.I., 602 S. 45th St., Omaha, NE 68106 **Case report: treatment of intractable sleepwalking.** Psychiatric Journal of University of Ottawa 5(2):86-88, 1980.

The case history is presented of an adult male with chronic, destructive, virtually intractable sleepwalking symptoms, treated with diazepam. The patient had previously been treated with a hypnotic conditioning paradigm as part of a larger study. He did not respond adequately, and some months later low doses of diazepam were instituted. The response was dramatic, positive, and followup after 1 year showed continued good responses. No indication of relapse or of tolerance to the diazepam is reported. It is suggested that the medication helps to stabilize and normalize sleep patterns. 10 references. (Author abstract modified)

004724 Salar, Giuseppe; Iob, Ivo; Mingrino, Salvatore. Istituto di Neurochirurgia della Universita di Padova, via Giustiniani 5,35100, Padua, Italy **Cortical evoked responses and transcutaneous electrotherapy.** Neurology. 30(6):663-665, 1980.

Pain induced by electrical stimulation of the median nerve at the wrist in six volunteers was clearly reduced by electrotherapy. Naloxone provoked a brief but immediate return of pain in four Ss, but caused a further decrease of painful sensation in two Ss. Somatosensory evoked potentials were significantly decreased during electrostimulation in all Ss. The cortical evoked responses returned to basal amplitude after naloxone in the four naloxone sensitive Ss but not in the other two Ss. 15 references. (Author abstract modified)

004725 Stein, Claudia L'Engle. University of Florida **The effects of medication and reading programs on the reading performance of hyperactive children. (Ph.D. dissertation).** Dissertation Abstracts International. 40(4):1917-B, 1979. Ann Arbor, Univ. Microfilms No. 7921944, 112p., 1979.

The differential effects of medication and academic programs on the reading comprehension and recognition achievement of 52 young hyperactive children were investigated. A 2 x 2 x 2 repeated measures analysis of variance indicates that an operant approach was significantly more effective than an eclectic approach in terms of final reading recognition and comprehension

achievement levels. There were no significant differences between medicated and nonmedicated groups in terms of final reading levels. There were no significant interaction effects among reading program, medication or time. It is concluded that the type of reading approach had a greater differential effect upon reading performance than did stimulant medication. (Journal abstract modified)

004726 Whalen, Carol K.; Henker, Barbara; Dotemoto, Sharon. Program in Social Ecology, University of California, Irvine, CA 92717 **Methylphenidate and hyperactivity: effects on teacher behaviors.** Science. 208(4449):1280-1282, 1980.

Teacher interactions with hyperactive and comparison boys were observed during classroom activities. A double-blind, methylphenidate placebo cross-over design was used within the hyperactive group. With no knowledge of any child's diagnosis or drug status, the teacher was more intense and controlling toward hyperactive boys taking placebo than toward either medicated hyperactive boys or comparison boys; her behavior did not differ toward the latter two groups. Discussion focuses on the need to consider the broad social ramifications of pharmacologic treatment programs. 78 references. (Author abstract)

004727 White, Kerrin; Bohart, Randy; Whipple, Katherine; Boyd, Jeffrey. Los Angeles County-University of Southern California Medical Center, 1934 Hospital Place, Los Angeles, CA 90033 **Lithium effects on normal subjects: relationships to plasma and RBC lithium levels.** International Pharmacopsychiatry. 14(3):176-183, 1979.

Lithium carbonate was administered to 15 normal Ss for 10 days in doses sufficient to produce plasma lithium concentrations in the range of 0.7 to 1.4mEq/1. Blood samples were taken periodically and analyzed for plasma and erythrocyte lithium concentration. Ss conpleted Profile of Mood States questionnaires on alternate days and listed side-effects. Ten Ss also completed three tests of psychomotor function at the beginning and end of the lithium trial. Results indicate that lithium induced dysphoric mood changes and psychomotor slowing, which were not significantly correlated with plasma or red blood cell lithium concentration. 16 references. (Author abstract modified)

004728 Wittenborn, J. R. Rutgers State University, New Brunswick, NJ 08903 **Behavioral toxicity of psychotropic drugs.** Psychopharmacology Bulletin. 16(2):66-68, 1980.

Research studies providing data concerning the behavioral toxicity of psychotropic drugs are reviewed, and considerations for the establishment of a standard assessment battery for assessing the minimal behavioral consequences of psychotropic drugs are discussed. The effects of hypnotic/sedative drugs and the benzodiazepines on reaction time, hand/eye coordination, tapping, visual perception, cancellation, card sorting, digit symbol substitution, and critical flicker fusion are described. It is apparent that different classes of psychotropic drugs have different patterns of behavioral effects in normal Ss, and that the form that behavioral toxicity assumes in response to psychotropic substances depends upon the nature of the substance. It is contended that the exact nature of the differential behavioral sensitivity to drugs will be best understood when a standard behavioral assessment battery is available and used in a standard manner with normal Ss. 8 references.

15 TOXICOLOGY AND SIDE EFFECTS

004729 Aanderud, S.; Strandjord, R. E. Strandjord: Dept. of Neurology, 5016 Haukeland sykehus, Bergen, Norway **Hypothyroidism induced by anti-epileptic therapy.** 61(5):330-332, 1980. Acta Neurologica Sandinavica.

Two patients on long-term antiepileptic drug therapy developed clinical hypothyroidism. One was being treated with carbamazepine and the other with phenytoin. Both became euthyroid and had normal thyroid hormone assays after the drugs were withdrawn. 8 references. (Author abstract modified)

004730 Allen, Marcia D. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA **Drug therapy in the elderly.** American Journal of Nursing. 80(8):1474-1475, 1980.

Special circumstances concerning drug therapy in the elderly are reviewed, and implications for geriatric nursing are discussed. Although many factors may increase the susceptibility of the elderly to the pharmacological action of many drugs, the three main factors that may decrease the biotransformation and excretion of drugs and increase and prolong the effects of drugs in elderly patients are decreased renal function, decreased hepatic function, and altered protein binding. Also, with increased age, there is an increase of body fat, which can lead to accumulation and prolongation of action of highly lipid soluble drugs. It is also thought that the blood-brain barrier may become more permeable with aging, permitting more drug to pass into the cerebrospinal fluid and possibly increase the likelihood of toxicity. 16 references.

004731 Amin, M. M.; Khan, P.; Lehmann, H. E. Clinical Research Unit, Lakeshore General Hospital, Pointe Claire, Quebec, Canada **The differential effects of viloxazine and imipramine on performance tests: their relationship to behavioural toxicity.** Psychopharmacology Bulletin. 16(3):57-58, 1980.

The differential effects of viloxazine, a tetrahydrooxazine, a bicyclic compound with antidepressant effects and a different side-effect profile than the tricyclic antidepressants, and imipramine on performance tests were investigated, and their relationship to behavioral toxicity was examined. A 4 week double-blind study of 20 patients with unipolar endogenous depression is described. Patients were tested on the Verdun Psychophysical Test Battery and on the Tartu Psychophysical Battery prior to and at the end of the 4 week treatment. While administration of viloxazine is associated with improvement in some perceptual and pure motor speed components of the performance test battery, administration of imipramine is associated with further impairment on these tests as well as in simple and more complex psychomotor performance. This difference is attributed to fewer muscarinic side-effects of viloxazine. 7 references.

004732 Bader, Ted F.; Newman, Karin. 3930 Harrison Street, Apt. F., Riverside, CA 92503 **Amitriptyline in human breast milk and the nursing infant's serum.** American Journal of Psychiatry. 137(7):855-856, 1980.

The excretion of amitriptyline and its metabolite, nortriptyline, in human breast milk of a woman taking amitriptyline chronically, and in the serum of the nursing infant were investigated. Although 151ng/ml of amitriptyline was found both in serum and milk of the motor, no tricyclics were detected in the infant's serum. The virtually equal levels of amitryptyline and nortriptyline in the mother's serum and milk indicate that these drugs are probably passed from serum to breast milk in a passive manner. On the basis of this clinical study, it was recommended to the mother than she continue breastfeeding her child if she so desired. The need for large-scale investigation of excretion of psychotropic drugs in human milk is noted. 4 references.

004733 Basavaraju, Nerlige G.; Wolf-Klein, Gisele; Silverstone, Felix A.; Libow, Leslie S. Jewish Institute for Geriatric Care, 271-11 76th Ave., New Hyde Park, NY 11042 **Cimetidine-induced mental confusion in elderly.** New York State Journal of Medicine. 80(8):1287-1288, 1980.

Case reports of two elderly patients who become confused with the administration of cimetidine and improved with cessation of therapy are presented. Cimetidine is a specific histamine H2 (hydrogen-2) receptor antagonist. There have been scattered reports of mental confusion, particularly among elderly patients. This susceptibility of the elderly may be partly due to impaired renal function during senescence since cimetidine is excreted unchanged through the kidneys. Further studies in pharmacokinetics are needed to determine the therapeutic dosage for the elderly, especially in those with renal impairment. 10 references.

004734 Bilikiewicz, A.; Januskiewicz-Grabiasowa, A.; Deptulski, T.; Taraszkiewicz, W.; Wojtowicz, M. Wojtowicz: Dept. of Cardiology, Institute of Internal Diseases, Gdansk, Poland **Changes in the electrocardiogram during treatment with tricyclic antidepressant drugs in endogenous depression.** Agressologie. 20(D):287-289, 1979.

ECG changes were investigated during the course of treatment of endogenous depression with moderate doses of tricyclic antidepressants. In 52 patients with endogenous depression, ECG readings were taken once a week during therapy and immediately after termination. Subjects included 39 patients with normal pretreatment ECGs and 13 with pretreatment ECG abnormalities. Changes of the ECG patterns were found in 17 cases during the treatment. These were elevation or lowering of the ST segment and flattening or inversion of the T-inflection, disturbances of the heart rhythm. They were most marked in patients receiving amitryptiline, maprotline, and lopramine and less marked in those receiving imipramine. The ECG changes became more intense with increases in dosage of tricyclic antidepressants, and at the end of the therapy they decreased. 1 reference. (Author abstract modified)

004735 Bjorndal, Niels; Casey, Daniel E.; Gerlach, Jes. Gerlach: Sct. Hans Hospital, Dept. H, DK-4000 Roskilde, Denmark **Enkephalin, morphine, and naloxone in tardive dyskinesia.** Psychopharmacology. 69(2):133-136, 1980.

Eight psychiatric patients with tardive dyskinesia (TD) were treated with single doses of the synthetic met-enkephaline analogue FK 33-824, morphine, and naloxone. The drug effects were assessed by blind evaluation of randomly sequenced videotapes made before and during treatment. FK 33-824 slightly reduced TD and increased preexisting bradykinesia. The effect on TD, however, was pronounced only in patients concurrently treated with neuroleptics in relatively high doses. Morphine had a similar although weaker antihyperkinetic effect, whereas naloxone had no effect. Side-effects of FK 33-824 included dizziness, heaviness in the extremities, slurred speech, and dryness of mouth. Morphine caused drowsiness, dizziness, ataxia, and nausea, and naloxone had no side-effects. The results do not point to a primary role of enkephalin in the pathophysiology of TD, but enkephalin may interact with dopamine functions and potentiate some of the effects of neuroleptic drugs. 24 references. (Author abstract modified)

004736 Booker, Harold E.; Goodfriend, Theodore L.; Tewksbury, Duane A. Goodfriend: William S. Middleton Memorial Veterans Hospital, 2500 Overlook Terrace, Madison, WI 53705 **Plasma renin concentration and phenobarbital levels in patients with epilepsy.** Clinical Pharmacology and Therapeutics. 26(6):715-717, 1979.

Plasma renin activity, renin concentration, and renin substrate were measured in patients on long-term anticonvulsant medication. An inverse correlation was observed between phenobarbital levels and reinin activity or concentration. There was a positive correlation between phenobarbital and renin substrate. Since elevation of renin substrate should have resulted in increased renin activity, it is possible that phenobarbital not only induces renin substrate synthesis but also supresses renin release. 10 references. (Author abstract modified)

004737 Christiansen, Claus; Baastrup, Poul C.; Transbol, Ib. Dept. of Clinical Chemistry, Glostrup Hospital, DK-2600 Glostrup, Denmark **Development of therapy: longitudinal study.** Neuropsychobiology. 6(5):280-283, 1980.

The development of primary hyperparathyroidism during lithium therapy was investigated in a longitudinal study of 13 manic-depressive patients. The bone mineral content and the serum levels of immunoreactive parathyroid hormone, and protein corrected calcium and magnesium were measured before and during treatment with lithium. Initially all four parameters were normal, but during treatment the bone mineral decreased and serum levels of immunoreactive parathyroid hormone, calcium, and magnesium increased. Although altered metabolism of parathyroid hormone cannot be ruled out, these data, together with other observations, suggest that a mild primary hyperparathyroidism sets in quite early after institution of lithium therapy. 15 references. (Author abstract modified)

004738 Cooperstock, Ruth. Addiction Research Foundation, Toronto, Ontario, Canada **Special problems of psychotropic drug use among women.** Canada's Mental Health. 28(2):3-5, 1980.

The special problems of women which lead to high consumption of psychotropic drug use, and the problems women encounter following use of these substances are examined. Problems encountered as a result of drug use include dependence; cross-addiction; cognitive, intellectual, and psychomotor deficits; the side-effects of hypnotic drugs such as flurazepam; and economic, social, and personal costs. When examining motives for drug use, it was found that the strains within family groups resulted in drug use by female rather than male informants. Tranquilizer use seemed particularly prevalent among women in role conflict. Women surveyed complained of extreme role strain, inability to comply with traditional expectations, and the lack of a right to express their dissatisfactions and preferences. The need to find a constructive alternative to drug use, one which may involve a structural change in drug users' lives, is viewed as a problem which both professional and lay members of the society should address. 30 references.

004739 Daneshmend, T. K.; Scott, G. L.; Bradfield, J. W. B. Bristol Royal Infirmary, Bristol BS2 8HW, England **Angiosarcoma of liver associated with phenelzine.** British Medical Journal. No. 6179:1679, 1979.

A case report is presented of a 64-year-old woman who exhibited angiosarcoma of the liver associated with phenelzine. The subject, admitted for investigation of anemia, gave a 4 month history of malaise, bruising tendency, and cough productive of small blood clots. She had been taking phenelzine for at least 6 years. It is noted that phenelzine given to female Swiss mice significantly increased the incidence of angiosarcoma at various sites, including the liver. Although such an association in a patient has not been recorded before, this may represent a failure in documenting drug history. 4 references.

004740 Elizur, Avner; Liberson, Zvi. Shalvata Psychiatric Center, P.O. Box 94, Hod Hasharon, Israel **An acute psychotic episode at the beginning of clonidine therapy.** Progress in Neuro-Psychopharmacology. 4(2):211-213, 1980.

A case of an acute behavioral/psychotic side-effect to clonidine therapy is presented, and a possible mechanism of this psychotic side-effect involving the adrenergic system is suggested. Conspicuous aspects of this episode in a 40-year-old woman are an abrupt onset and short duration of symptoms, with a com-

plete return to premorbid level of psychosocial adjustment. The symptoms resembled schizophrenia, although a toxic psychosis due to an organic brain syndrome cannot be ruled out. It is suggested that clonidine has substantial presyntptic agonist effects at the alpha-receptor leading to a decrease in the release of noradrenalin, and that this decrease is related to the described effects. 12 references. (Author abstract modified)

004741 Floru, Lucien; Tegeler, J.; Wolmsen, H. Psychiatrische Klinik der Universitat Dusseldorf, Bergische Landstrasse 2, D-4000 Dusseldorf 12, Germany **/Treatment of lithium induced tremor with the beta-receptor blocker pindolol./** Die Behandlung des Lithiumtremors mit dem Beta-Rezeptorenblocker Pindolol. International Pharmacopsychiatry. 14(3):149-157, 1979.

The effects of pindolol (15mg/day) and placebo on lithium induced tremor were compared in a 4 week crossover study of 22 patients, age 20 to 65 years, who were treated with lithium carbonate (Quilonum Retard). Tremor was measured twice a week by a self-evaluation rating scale and by three apparative methods (accelerometer, hole plate, and aimed tapping plate). A significant therapeutic effect of pindolol on lithium induced tremor was reflected in the self-evaluations and in the hole plate test. 20 references. (Journal abstract modified)

004742 Gardos, George; Cole, Jonathan O. Institute for Research and Rehabilitation, 591 Morton St., Boston, MA 02124 **Overview: public health issues in tardive dyskinesia.** American Journal of Psychiatry. 137(7):776-781, 1980.

Public health issues in tardive dyskinesia are reviewed, and strategies for prevention are identified. The incidence of tardive dyskinesia is unknown, and prevalence rates yield conflicting and possibly misleading estimates. The natural course of tardive dyskinesia is highly variable; in some patients (probably many fewer than previously believed) it is irreversible. No currently available therapeutic agent satisfies the criteria of safety, marked effectiveness, and prolonged efficacy in the treatment of tardive dyskinesia. Primary prevention involves reducing antipsychotic drug exposure, secondary prevention involves early diagnosis and prompt intervention, and tertiary prevention involves clinical measures to reduce disability and to treat severe cases vigorously. It is contended that educational methods that disseminate knowledge and influence prescribing habits need to be identified and used more widely. 46 references. (Author abstract modified)

004743 Gerner, Robert H.; Psarras, James; Kirschenbaum, Michael A. 760 Westwood Plaza, Los Angeles, CA 90024 **Results of clinical renal function tests in lithium patients.** American Journal of Psychiatry. 137(7):834-837, 1980.

Results of extensive noninvasive testing of renal function in 43 affective disorder patients who had been taking lithium for 1 to 120 months are described. The only abnormal finding is that the urine concentrating ability of these patients is moderately, but asymptomatically impaired. It appears that plasma creatinine and blood urea nitrogen alone are not sensitive enough to use as screening tests for patients receiving lithium because they do not correlate well with the slight abnormalities in creatinine clearance or 24 hour urine protein excretion that were observed in a few patients. It is concluded that there is not enough evidence to justify not initiating or continuing lithium use in patients who might benefit from it. 27 references. (Author abstract modified)

004744 Glazer, William M.; Moore, Daniel C. Connecticut Mental Health Center, 34 Park St., New Haven, CT 06508 **The diagnosis of rapid abnormal involuntary movements associated with fluphenazine decanoate.** Journal of Nervous and Mental Disease. 168(7):439-441, 1980.

Three patients with low grade tardive dyskinesia who developed an acute episode of abnormal involuntary movements after a single injection of fluphenazine decanoate are discussed. In all three patients, symptoms were relieved after treatment with antiparkinsonian medication. The differential diagnosis of these movements is discussed, and a possible animal model for this phenomenon is described. These observations suggest that the phenomenology of neuroleptic induced abnormal involuntary movements may be more heterogeneous than originally believed. 5 references. (Author abstract modified)

004745 Gross, Michael L. P. Royal Free Hospital, London NW3 2Q3, England **Acute dystonia as idiosyncratic reaction to haloperidol.** Lancet. 2(8192):479-480, 1980.

The case of a 12-year-old girl with no personal or family history of neurological disorder and who developed acute dystonia as an idiosyncratic reaction to haloperidol is reported. The patient, with chronic rhinitis, was given disodium cromoglycate and haloperidol 1.5mg twice a day as a sedative. After the fifth dose of haloperidol on the third day, an acute dystonic syndrome developed. It is reported that anicholinergic drugs are helpful in reversing these acute syndromes. In this patient intravenous diazepam rapidly brought relief. The patient has been advised to avoid other antidopaminergic drugs, including metoclopramide and prochlorperazine. It is recommended that the use of these drugs in the adolescent should be avoided. 2 references.

004746 Hargreaves, William A.; Gaynor, Jessica. University of California, San Francisco, School of Medicine, Dept. of Psychiatry, San Francisco, CA **Risk of tardive dyskinesia: preliminary hypotheses.** Psychopharmacology Bulletin. 16(2):48-50, 1980.

A mathematical model of hypothetical relationships of drug prescription history to the incidence and prevalence of abnormal involuntary movement or tardive dyskinesia (TD), which employs both biological and epidemiological concepts, is described. To examine the mathematical operation of the model, two computer programs were written that incorporate these equations. The first program models accumulating risk of TD over a period of years, while the second program models short-term effects of drug discontinuation on symptom suppression. Each program accepts a drug history in the form of mean daily dose of an antipsychotic drug during successive time periods, along with its associated potency and compliance factors. Given assumed values of each parameter, the program calculates for this drug history an estimated relative risk of TD for each time period. 6 references.

004747 Haruda, Fred. Box 133, Neurological Institute, Columbia Presbyterian Medical Center, 710 West 168 St., New York, NY 10032 **Phenytoin hypersensitivity: 38 cases.** Neurology. 29(11):1480-1485, 1979.

A review of 38 cases of phenytoin hypersensitivity showed that most of the reactions occurred within 2 months of the start of therapy. Rashes were the most frequent manifestations of phenytoin hypersensitivity,, followed by fever, lymphadenopathy, eosinophilia, abnormal liver function, blood dyscrasias, serum sickness, renal failure, and polymyositis. The pseudolymphoma syndrome (fever, rash, and lymphoadenopathy) occurred in nine patients. It is suggested that serious morbidity from phenytoin hypersensitivity can be prevented by early recognition of the reactions, prompt drug withdrawal, and appropriate therapeutic action. 43 references. (Author abstract modified)

004748 Hendler, Nelson; Cimini, Cindi; Ma, Terence; Long, Donlin. Mensana Clinic, Greenspring Valley Rd., Stevenson, MD 21153 **A comparison of cognitive impairment due to benzo-**

diazepines and to narcotics. American Journal of Psychiatry. 137(7):828-830, 1980.

Cognitive impairment associated with benzodiazepines and narcotics was investigated among 106 consecutive admissions to a chronic pain treatment center. All Ss were administered an EEG, the WAIS, Memory Quotient, and Bender Gestalt tests. Patients receiving benzodiazepines alone demonstrated alterations in cognitive functioning and EEG evidence of a sedative effect. Patients receiving narcotics alone and a group of patients not receiving medication did not show signs of cognitive impairment. The effects of benzodizepines on sleep and perception of chronic pain, in combination with the cortical changes that they produce, imply that these drugs should not be used in most patients with chronic pain. 12 references. (Author abstract modified)

004749 Hoschl, C. Psychiatricka Klinika, 8-Bohnice, 181 03 Prague, Czechoslovakia **/Glucocorticoids and mental alterations./** Glukokortikoidy a psychicke zmeny. Prakticky Lekar. 59(17):647-648, 1979.

Changes in the mental condition of patients treated with glucocorticoids are discussed. The most frequent symptoms are emotional disorders, such as depressions and mania. Similar disorders accompany dysfunctions of suprarenal glands of any origin. Glucocorticoids have a feedback effect within the hypophysis, hypothalamus, and other areas of the brain. Psychiatric complications are rare during treatment with glucocorticoids and do not seem to depend on the amount of the dose. At any rate, even serious psychotic conditions occurring during such treatment are reversible. It is concluded that if the attending physician is familiar with the risks and can provide psychiatric supervision in cases requiring treatment with glucocorticoids because of some other serious ailment, mental disorders do not represent a strict counterindication of the treatment. 13 references.

004750 Howe, J. G. Dept. of Medicine, St. James' University Hospital, Leeds LS9 7TF, England **Lorazepam withdrawal seizures.** British Medical Journal. No. 6224:1163-1164, 1980.

Two case studies of seizures after lorazepam withdrawal are reported. Both patients had taken lorazepam for years and in each case abrupt withdrawal produced unpleasant symptoms and a seizure. 3 references.

004751 Huang, Chuong C.; Wang, Richard I. H.; Hasegawa, Andrew; Alverno, Luca. Dept. of Psychiatry, Medical College of Wisconsin, Madison, WI **Evaluation of reserpine and alpha-methyldopa in the treatment of tardive dyskinesia.** Psychopharmacology Bulletin. 16(3):41-43, 1980.

The efficacy of reserpine and alpha-methyldopa for the treatment of tardive dyskinesia (TD) was assessed in a double-blind study of 30 Veterans Administration inpatients manifesting TD secondary to antipsychotic medications. In this study, neuroleptic and anticholinergic medications were kept at the same level, and the manifestations of TD were controlled by moderate doses of reserpine or alpha-methyldopa. None of the previously reported side-effects or alpha-methyldopa or reserpine, such as gastric ulcer, depression, psychotic agitation, and blood dyscrasia, were observed. 12 references.

004752 Krakiewicz, Adam; Kiejna, Andrzej. Klinika Psychiatryczna AM, ul. Kraszewskiego 25, 50-229 Wroclaw, Poland / **Complications in the central nervous system during lithium therapy./** Powiklania ze strony osrodkowego ukladu nerwowego w czasie terapii litem. Psychiatria Polska. 14(1):63-67, 1980.

Complications observed in the central nervous system during lithium therapy are discussed with emphasis on neurological symptoms, psychopathological indications, and general symptomatology. Neurological disturbances encompass such pathomechanisms as ataxia, nystaxis, muscular stiffness, muscular hypotonia, tremors, diskinesia, facial mask, drooling, polydipsia, polyuria, aphasia, and grand mal attacks. Psychopathological symptoms discovered in association with lithium therapy include disturbances in consciousness, sleepiness, hallucinations, and confusion. More general physical symptoms include: weakness, loss of body heat, low blood pressure, nausea, and vomiting. It is suggested that particular care should be taken in the treatment of patients with somatic illnesses, particularly in those with disturbances in water electrolytic systems. In the treatment of neurological symptoms resulting from lithium treatment, intravenous infusion of NaCl, as well as eufiline, and natrium bicarbonate, have been used to alleviate the renal clearing of lithium. In addition, antiparkinson mediums, hydantoin derivatives, vitamin B comple, and other internal drugs have been used. 31 references. (Journal abstract modified)

004753 Kulik, Frank A.; Wilbur, Robert; Kruckeberg, Myrna. Wilbur: 125 West 96th Street, New York, NY 10025 **Clinical experience with fluotracen HCl: report of a case.** Progress in Neuro-Psychopharmacology. 3(5/6):559-561, 1979.

A case report of a depressed patient who experienced excellent initial response to fluotracen HCl, a new thymoneuroleptic, is presented. The patient then developed a syndrome of amphetamine like hyperstimulation which necessitated discontinuation of the medication. Rapid, marked deterioration ensued. Hyperstimulation and agitation have not been described previously for fluotracen. Another group found that this drug is rapidly effective, even in treatment refractory patients, but that premature termination of therapy can provoke a rapid relapse. Fluotracen is discussed in relation to other neuroleptics and thymoleptics, and it is suggested that comparative studies with thiothixene might be informative. 4 references. (Author abstract modified)

004754 Kulik, Frank A.; Wilbur, Robert. Wilbur: 125 West 96th Street, New York, NY 10025 **Propranolol for tardive dyskinesia and extrapyramidal side effects (pseudoparkinsonism) from neuroleptics.** Psychopharmacology Bulletin. 16(3):18-19, 1980.

Three case reports of the use of propranolol for tardive dyskinesia (TD) and extrapyramidal side-effects (EPS) (pseudoparkinsonism) from neuroleptic are presented. Owing to the long history of neuroleptic usage by these patients, it seems highly probable that their TD and EPS are drug related. It is noted that the coexistence of IPS and TD poses difficult clinical problems, since both disorders are associated with the extrapyramidal tract, but Parkinsonism is thought to arise from a deficiency of dopamine and a subsequent predominance of anticholinergic over dopaminergic activity, while TD is thought to result from a neuroleptic induced hypersensitization of postsynaptic dopaminergic receptors in the striatum. Results in these three cases indicate that propranolol is similarly effective in EPS and TD. 3 references.

004755 Lechin, Fuad, Gomez, Francisco; van der Dijs, Bertha; Lechin, Ernesto. Apartado 80.983, Caracas 1080 A, Venezuela **Distal colon motility in schizophrenic patients.** Journal of Clinical Pharmacology. 20(7):459-464, 1980.

The effects of the dopaminergic blocking agents haloperidol and sulpiride on distal colon motility were studied in 30 chronic schizophrenic patients. Although these drugs inhibit distal colon motility in most nonpsychotic Ss, sulpiride inhibited motility in only 10% of the schizophrenic Ss; haloperidol increased motility in 23.3% and had no effect in the other schizophrenic Ss. Dihydroergotamine, phentolamine, and clonidine inhibited distal colon motility in 90% of the schizophrenic patients, suggesting

peripherhal noradrenergic hyperactivity in these Ss. 25 references. (Author abstract modified)

004756 Lerer, B.; Birmacher, B.; Ebstein, R. P.; Belmaker, R. H. Jerusalem Mental Health Center, POB 140, Jerusalem, Israel **48-hour depressive cycling induced by antidepressant.** British Journal of Psychiatry. 137(August):183-185, 1980.

The occurrence of 48-hour rapid cycling in a 63-year-old man with recurrent unipolar depression after treatment with dibenzepin (Noveril), an atypical tricyclic antidepressant, is reported. After discontinuation of the dibenzepin, the cycling disappeared and the patient was extremely depressed during the 6 day drug free period and also while receiving placebo for 4 days. When dibenzepin was reinstituted, there was no response for 4 days but thereafter a more attenuated, less regular cycling pattern began to develop. Twenty four hour urinary cyclic adenosine monophosphate excretion was elevated during both periods of rapid cycling but showed no clear day to day correlation with cyclic mood changes. Clinicians should be aware that rapid cycling may be an iatrogenic phenomenon rather than an especially drug resistant form of affective illness, and that such rapid cycling may occur even with atypical antidepressants. 13 references.

004757 MacCallum, W. A. G. Purdysburn Hospital, Saintfield Road, Belfast BT8 8BH, Northern Ireland **Interaction of lithium and phenytoin.** British Medical Journal. No.6314:610-611, 1980.

The development of a lithium type toxicity during combined lithium and phenytoin treatment, despite normal serum concentrations, is reported in a 48-year-old manic-depressive male with a history of grand mal seizures. When carbamazepine was substituted for phenytoin, polyuria, polydipsia, and tremor disappeared, the free thyroxin index reverted to normal. In addition, the patient commented that his libido had returned. Seemingly, in the presence of phenytoin, lithium salts at serum concentrations accepted as standard have toxic effects on the renal tubules, thyroid metabolism, and CNS centers related to tremor and libido. 2 references. (Author abstract modified)

004758 Mathew, Roy J.; Weinman, Maxine; Claghorn, James L. Psychosomatic Research Section, Texas Research Institute of Mental Sciences, Houston, TX **Tricyclic side effects without tricyclics in depression.** Psychopharmacology Bulletin. 16(3):58-60, 1980.

The frequency of side-effect symptoms in depression and pharmacological and nonpharmacological factors which influence their occurrence were investigated. The following rating scales and questionnaires were administered to 51 depressed patients and 51 control Ss: Eysenck Personality Inventory (EPI); Beck Depression Inventory (BDI); State-Trait Anxiety Inventory (STAI); a questionnaire concerning alcohol, cigarette, coffee, tea, and chewing gum consumption; a 27 item tricyclic side-effects questionnaire; and a personal data form. Implications for the prescribing physician of the finding that symptoms resembling tricyclic side-effects can occur in association with depression even in drug free patients are discussed. The inability to identify multivariate models of symptoms in relation to depression, state anxiety, trait anxiety, and neuroticism and the identification of two independent factors (symptoms, rating scale scores) strongly indicate that these symptoms are nonspecific responses to depressive illness. 6 references.

004759 Naber, Dieter; Steinbock, Herbert; Greil, Waldemar. Psychiatrische Klinik der Universitat Munchen, Nussbaumstrasse 7, D-800 Munich 2, Germany **Effects of short- and long-term neuroleptic treatment on thyroid function.** Progress in Neuro-Psychopharmacology. 4(2):199-206, 1980.

Parameters of thyroid function were measured in nine acute schizophrenic patients before and during neuroleptic treatment and in 22 chronic schizophrenic patients, hospitalized and treated with neuroleptic drugs for 6 to 21 years. Neither thyroxine and triiodothyronine nor basal and stimulated thyrotropin (TSH) serum levels were changed significantly by the acute neuroleptic treatment. In the chronic patients, the mean values of thyroxine and thyroxine binding globuline as well as of basal and stimulated TSH were all within the normal range. These data suggest that neuroleptic drugs do not markedly interfere with thyroid function. 40 references. (Author abstract)

004760 Nasrallah, Henry A.; Pappas, Nicholas J.; Crowe, Raymond R. Dept. of Psychiatry, College of Medicine, University of Iowa, Iowa City, IA 52240 **Oculogyric dystonia in tardive dyskinesia.** American Journal of Psychiatry. 137(7):850-851, 1980.

A case report on an oculogyric dystonic reaction in a chronically medicated patient with severe tardive dyskinesia of several years' duration is presented. The possibility that dystonia may be due to increased dopamine activity is discussed in relation to the clinical picture of dystonia superimposed on tardive dyskinesia. It is speculated that dystonia is the acute, transient, extrapyramidal manifestation of increased dopamine hyperactivity through a rebound increase in dopamine release. In the present case, the addition of reserpine to trifluoperazine 2 days before the dystonic reaction is consistent with Marsden's hypothesis of dopamine hyperactivity preceding dystonia. 11 references.

004761 Ochs, Hermann R.; Carstens, Gerhard; Greenblatt, David J. Medizinische Universitatsklinik, D-5300-Venusberg, Germany **Reduction in lidocaine clearance during continuous infusion and by coadministration of propranolol.** New England Journal of Medicine. 303(7):373-377, 1980.

The influence of prolonged infusion of lidocaine and of coadministration of propranolol on the clearance of lidocaine in healthy subjects were examined. After single doses of lidocaine, all subjects had dysphoric sensations, including drowsiness, lethargy, paresthesias of the hands and mouth, and hyperacusis. During continuous infusion, subjects had the dysphoric sensations as well as general malaise. The coadministration of propranolol significantly impaired the half-life and clearance of lidocaine. This effect is probably attributable to a reduction in cardiac output and hepatic blood flow due to propranolol induced beta blockade. 15 references.

004762 Osifo, Nosakhare G. Dept. of Pharmacology and Toxicology, University of Rochester Medical Center, 601 Elmwood Ave., Rochester, NY 14642 **Drug-related transient dyskinesias.** Clinical Pharmacology and Therapeutics. 25(6):767-771, 1979.

The mechanism and treatment of drug induced dyskinesias are discussed, with emphasis on movement disorders caused by antimalarial agents such as chloroquine and amodiaquine. Chlorpromazine, diazepam, diphenhydramine, and methocarbamol have been used to treat these dyskinesias, but their effectiveness has not been established. The transient drug induced dyskinesias may reflect brief derangements in extrapyramidal control due to excess dopamine in the basal ganglia, whereas persistent dyskinesias may involve supersensitive dopaminergic postsynaptic receptors. 29 references.

004763 Palva, E. S.; Linnoila, M.; Saario, I.; Mattila, M. J. Dept. of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Acute and subacute effects of diazepam on psychomotor skills: interaction with alcohol.** Acta Pharmacologica et Toxicologica. 45(4):257-264, 1979.

The effects of diazepam (5, 10, and 20mg) and alcohol (0.5, 0.8, and 1.2g/kg) on psychomotor skills were studied in 200 healthy students. All doses of alcohol impaired divided attention and the largest dose also impaired coordination. Diazepam impaired reactive and coordinative skills when given in combination with alcohol, but not when given alone. In a second study, 18 Ss were given 2 or 10mg diazepam three times a day for 2 weeks and tested for psychomotor skills on days 7 and 14. Ss treated with 10mg diazepam showed increased reaction times, as well as impaired coordination and attention. The 2mg group did not differ from placebo controls. Alcohol did not enhance the effects of diazepam in these Ss, suggesting that tolerance to diazepam may compensate for the deleterious interaction of diazepam and alcohol seen in the acute study. 19 references. (Author abstract modified)

004764 Pandurangi, A. K.; Devi, Vasundhara; Channabasavanna, S. M. Presidential Plaza, Apt. 901, 600 East Genesee Street, Syracuse, NY 13202 **Caudate atrophy in irreversible tardive dyskinesia (a pneumoencephalographic study).** Journal of Clinical Psychiatry. 41(7):229-231, 1980.

Pneumoencephalography was conductd under standard conditions on five patients with tardive dyskinesia and three matched controls to obtain evidence of caudate atrophy. Atrophy was observed in three patients, who also proved refractory to treatment of their dyskinesia. It is concluded that tardive dyskinesia is a heterogenous entity, with some patients having irreversible dyskinesia and exhibiting radiologically demonstrable damage. The findings have implications for study of neurological syndromes associated with antipsychotic drug treatment for such conditions as schizophrenia and epileptic psychosis. 12 references. (Author abstract modified)

004765 Pratt, Thomas H. Dept. of Medicine, Baptist Memorial Hospital, Memphis, TN 38104 **Rifampin-induced organic brain syndrome.** Journal of the American Medical Association. 241(22):2421-2422, 1979.

A case study is reported in which acute organic brain syndrome was associated with rifampin administration in the treatment of pulmonary tuberculosis. The patient experienced episodes of confusion, disorientation, and agitation, which increased in both frequency and duration. When rifampin therapy was discontinued, an improvement in mental status was noted within 72 hours and notable improvement both clinically and on EEG occurred within six days. Other side-effects of rifampin administration are also discussed. 9 references.

004766 Racy, John; Ward-Racy, E. Ann. Dept. of Psychiatry, University of Arizona, College of Medicine Tucson, AZ 85724 **Tinnitus in imipramine therapy.** American Journal of Psychiatry. 137(7):854-855, 1980.

Four case reports of tinnitus associated with imipramine therapy are presented, and the brief clinical literature concerning reports of tinnitus associated with tricyclic anti-depressant administration is reviewed. It is concluded that tinnitus may not be as rare a side-effect of tricyclic therapy as would appear from the literature. The fact that these four patients were able to continue with and profit from such therapy (either on a reduced dose of imipramine or with a substitute) suggests that this side effect is not a serious impediment or contraindication to tricyclic use. Tinnitus is very distressing to patients but bares no resemblance to hallucinations. Reduction in dosage of imipramine was usually sufficient to control the tinnitus. 9 references.

004767 Savolainen, Kai. Institute of Occupational Health, Dept. of Industrial Hygiene and Toxicology, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland **Combined effects of xylene and alcohol on the central nervous system.** Acta Pharmacologica et Toxicologica. 46(5):366-372, 1980.

Ten healthy male Ss were exposed to 6 or 11.5mcmol/1 m-xylene after a single dose of 0.4 or 0.8g/kg alcohol. The higher concentration of xylene tended to impair reaction time and body balance, but the effect was not significant. Alcohol caused a dose dependent impairment. The deleterious effects of xylene and alcohol were usually additive, but the higher concentration of xylene antagonized the effects of alcohol on body balance. 21 references. (Author abstract modified)

004768 Schanda, H.; Saletu, B. Psychiatrische Universitats-Klinik, Lazarettgasse 14, A-1090 Vienna, Austria /**Repolarization disturbances in the ECG under antidepressant drugs. A comparison of two drugs differing in chemical structure and pharmacological profile.**/ Zur Frage der Spezifitat von Repolarisationsdstorungen im EKG unter Psychopharmaka. Eine Gegenuberstellung zweier in chemischer Struktur und Wirkingsmechanismus differenter antidepressiv wirkender Substanzen. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(4):338-345, 1980.

In connection with clinical drug trials (n=20), repolarization disturbances in ECG recordings were compared in two antidepressant drugs differing in chemical structure and pharmacological profile: tandamine (AY 23946), a tricyclic with main effects on norepinephrine reuptake; and fluvoxamine (DU 23000) a nontricyclic antidepressant with a selective effect on serotonin reuptake. No differences were observed regarding either frequency or pattern of the repolarization disturbance. It appears that the chemical structure of the drug is not responsible for the typical form of the repolarization disturbances. It is hypothesized that toxic effects and regulatory mechanisms of the cardiovascular system, caused by changes in norepinephrine and 5-hydroxytryptamine levels may be responsible for the aforementioned ECG abberrations. 34 references. (Journal abstract modified)

004769 Smith, Robert E.; Low, Nancy N.; Nasrallah, Henry A. Dept. of Psychiatry, College of Medicine, University of Iowa, 500 Newton Road, Iowa City, IA 52242 **Haloperidol and an unrelated sudden death.** American Journal of Psychiatry. 137(7):843-844, 1980.

A case report of the sudden, unexpected death in a young man who had received only moderate doses of haloperidol for control of extreme agitation is presented. An autopsy was performed but the cause of death was not determined until a detailed reexamination of the patient's heart was undertaken. It was found that death occurred during acute congestive heart failure, and was caused by acute myocardial ischemia with severe segmental coronary atherosclerosis present. It is noted that when sudden, unexpected deaths occur in psychiatric patients, the psychotropic medications the decedent had been receiving are often suspected of causing or contributing to the fatality. 8 references.

004770 Stewart, Ronald B.; Karas, Barry; Springer, Philip K. Dept. of Clinical Pharmacy, College of Pharmacy, University of Florida, J. Hillis Miller Health Center, Gainesville, FL **Haloperidol excretion in human milk.** American Journal of Psychiatry. 137(7):849-850, 1980.

A case report documenting the excretion of haloperidol in human milk is presented, and implications for treatment are discussed. Levels of haloperidol in the breast milk were 5ng/ml following a 12mg dose. Since an infant normally ingests from one half to one and one half liters of milk daily, the infant could receive a maximum of 0.0075ng/day of haloperidol. Although these are very small absolute amounts, the effect of these small

concentrations of haloperidol on an infant is not known. Therefore, physicians should carefully assess the need for antipsychotic drug therapy in a mother nursing her infant. 9 references.

004771 Straker, M. Brentwood V.A. Medical Center, Los Angeles, CA 90073 **Clinical factors in tardive dyskinesia.** Psychiatric Journal of the University of Ottawa. 5(1):28-33, 1980.

Clinical factors in tardive dyskinesia, an iatrogenic disorder associated with prolonged high dose neuroleptic schedules, are discussed. The dyskinesia often involves tongue, mouth, and face. The abnormal athetoid movements are usually assessed by clinical rating scales. Suspected risk related variables include old age, cerebral organicity, duration of treatment, and the total amount of drug ingested. Data suggest that the pathogenesis is related to a dopamine receptor denervation hypersensitivity or to a dopaminergic cholinergic imbalance, but there is no firmly established etiology nor is there a specific curative therapy. Management principles focus upon immediate withdrawal of anticholinergics and a gradual phased decrease of neuroleptics. Restraint in drug prescribing aims at establishing minimal neuroleptic dosages which are therapeutic, using anticholinergics sparingly and intermittently, and supervising medication withdrawal at the earliest sign of tardive dyskinesia. 77 references. (Author abstract modified)

004772 Tanaka, Katsuyuki; Kameda, Hideaki; Sugita, Yoshiro; Hishikawa, Yasuo. Psychiatry Dept, Osaka Prefectural Hospital, Osaka, Japan **A case with pentazocine dependence developing delirium on withdrawal.** Psychiatria et Neurologia Japonica. 81(4):289-299, 1979.

A case of pentazocine dependence developing a delirious state on sudden withdrawal is presented. A patient who had received daily injections of pentazocine for over six years developed a delirious state on the third night of withdrawal at the psychiatric ward of a general hospital, with symptoms lasting for six days. This delirious state resembled delirium tremens in chronic alcoholics or withdrawal delirium observed in meprobamate addicts, and was characterized by tremulousness, visual hallucinations, disorientation, disturbance of rapport, clouding of consciousness and severely disturbed behavior. Polygraphic recording of nocturnal sleep taken soon after disappearance of the delirious state was characterized by concomitant appearance of a low voltage fast and slow mixed frequency EEG, REM, and tonic discharge in the mental muscles. This state called stage 1-REM with tonic EMG is considered to be due to dissociation of REM sleep mechanism. 22 references. (Journal abstract modified)

004773 Tondlova, H.; Vrzal, K.; Bastecky, J.; Boleloucky, Z. Boleloucky: Jihlavska 102, Brno, Czechoslovakia **Tricyclic antidepressants and distortions of urination in men.** Agressologie. 20(D):291-293, 1979.

The relationship between treatment with tricyclic antidepressants and the incidence and severity of urological symptoms was investigated. Subjects were 46 male outpatients aged 45 to 72 with a diagnosis of endogenous or involutional depression. Fifteen patients had been treated with imipramine and 31 with dosulepine for a period of at least 4 weeks. Patients with no pretreatment urological difficulties did not develop any during treatment. On the other hand, 10 patients who showed pathological pretreatment findings on the prostate were affected by distortions of urination in the course of the treatment by both drugs (five cases with dosulepine and five cases with imipramine). In two of these patients acute urinary retention occurred, and in four cases an aggravation of the palpation finding took place in regard to hypertrophy or fibrotic changes. While a positive finding on the prostate is not seen as contraindication for tricyclic antidepressants, urological examination for all male patients over age 50 is recommended before beginning such treatment. 8 references.

004774 Ungvari, G.; Petho, B. Dept. of Psychiatry, University Medical School, Balassa 6, H-1083 Budapest, Hungary **Reversal of neuroleptic-induced stupor by procyclidin: two case reports and their theoretical implications.** Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(3):257-260, 1979.

Characteristics of pathogenic importance of neuroleptic induced stupor (NIS) are described, via an outline of two case reports and a review of the literature. The origin of NIS is discussed and fundamental clinical and experimental facts are presented, all of which emphasize the importance of the acute blockade of postsynaptic DA-ergic receptors. The significance of the possible relationship and similarity between NIS and catatonic stupor, and the theoretical possiblities this relationship offers is emphasized. 39 references. (Author abstract modified)

004775 Ungvari, Gabor. 1165 Centenarium K/3, Budapest, Hungary **Neuroleptic-related sudden death (proven or a mere hypothesis?).** Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(1):29-33, 1980.

The implication of neuroleptics in the sudden death of patients undergoing psychopharmacotherapy was investigated. Out of 11,935 patients treated with neuroleptics at one clinic over a period of 11 years, eight died suddenly and unexpectedly. The sudden death mortality rate of medicated patients was not higher than that of the general population of the same age distribution. A detailed analysis of the eight deaths produced some unusual findings, but their relationship to the neuroleptic effect requires further investigation. It appears that: 1) sudden death may occur in the case of haloperidol treatment; 2) cardiovascular hypoplasia without clinical symptoms may contribute to the risks; and 3) pulmonary embolism without primary focus was present in four cases. It is concluded that the role of neuroleptics as a possible sudden death risk factor may only be conjectured. 22 references. (Journal abstract modified)

004776 van Putten, Theodore; May, Philip R. A.; Marder, Stephen R. Dept. of Psychiatry, University of California, Los Angeles, CA 90024 **Subjective responses to thiothixene and chlorpromazine.** Psychopharmacology Bulletin. 16(3):36-38, 1980.

A method for assessing subjective responses of schizophrenic Ss to initial doses of thiothixene and/or chlorpromazine is described, and the possible deviant pharmacokinetics of Ss reporting a dysphoric reponse are discussed. Newly admitted schizophrenic patients were given an initial test dose of either chlorpromazine or thiothixene by mouth. Blood and saliva drug levels and subjective responses were measured over the test dose period prior to subsequent treatment with a controlled standardized course of drug therapy. A dysphoric response to a test dose of thiothixene was found to be a powerful and significant predictor of early noncompliance. Dysphoric responders experience significantly more extrapyramidal symptoms, notably akathisia, during the 24 hrs after their first dose. However, the fact that some syntonic responders also experienced extrapyramidal symptoms suggests that much depends on the emotional meaning and significance that a side-effect has for the individual patient. 8 references.

004777 Varma, Surendra K.; Messiha, F. S.; Sharma, Bharat, B. Dept. of Pediatrics, Texas Tech University Health Sciences Center, School of Medicine, Lubbock, TX 79430 **Neuro-endocrine effects of lithium carbonate therapy in Gilles de la Tourette's syndrome.** Research Communications in Psychology, Psychiatry, and Behavior. 5(2):219-229, 1980.

The neruoendocrine effects of lithium carbonate therapy in Gilles de la Tourette's syndrome were studied. There was evidence of mild central diabetes insipidus and decreased creatinine clearance during lithium therapy. There were blunted thyrotropin stimulating hormone (TSH) and prolactin responses to thyrotropin releasing hormone (TRH) which persisted for approximately 16 weeks after discontinuation of lithium therapy. Creatinine clearance and urinary concentrating capacity returned to normal after lithium carbonate was discontinued. If lithium therapy is monitored closely, diabetes insipidus and renal damage can be prevented. The same cannot be stated for lithium's effect on thyroid hormones. 24 references. (Author abstract modified)

004778 Wall, Robert; Linford, Susan M. J.; Akhter, Miftikhar. Regional Addiction Treatment Unit, All Saints' Hospital, Birmingham B18 5SD, England **Addiction to Distalgesic (dextropropoxyphene).** British Medical Journal. No. 6225:1213-1214, 1980.

A case study is reported of a 41-year-old woman who developed an addiction to Distalgesic, an analgesic containing dextropropoxyphene. Treatment consisted of withdrawing Distalgesic and giving methadone on a reducing scale. It is concluded that because of evidence indicating the prolonged administration of medications containing dextropropoxyphene leads to tolerance and dependence, these drugs should be reappraised. 4 references.

004779 Waters, Brent; Resnick, Maurice; Simeon, Jovan; Trites, Ronald; Fiedorowicz, Christina. Royal Ottawa Hospital, 1145 Carling Ave., Ottawa, Ontario, Canada K1Z 7K4 **An adverse reaction to piracetam in an hypothyroid 10 year old boy.** Progress in Neuro-Psychopharmacology. 4(2):207-209, 1980.

An adverse reaction to piracetam (Nootropil) in a 10-year-old boy receiving thyroid supplementation for secondary hypothyroidism is reported. The acute brain syndrome resolved rapidly upon discontinuation of piracetam but the same state was induced on further provocations with the compound. The absence of chemical laboratory results from the time of the provocations does not allow determination of whether these adverse effects were due to an impairment of thyroxin metabolism. It is urged that piracetam be administered with caution in the presence of hypothyroidism or thyroid supplementation until the nature of this apparent adverse reaction is elucidated. 4 references. (Author abstract modified)

004780 White, Kerrin; Cohen, Lawrence J.; Deandrea, Diana. Dept. of Psychiatry, Los Angeles County/University of Southern California Medical Center, 1934 Hospital Place, Los Angeles, CA 90033 **An unusual movement disorder associated with neuroleptic treatment: tardive dyskinesia?** Journal of Nervous and Mental Disease. 168(7):442-444, 1980.

A case report of a chronically psychotic man presenting signs of a movement disorder exacerbated by neuroleptic treatment and repeatedly diagnosed as tardive dyskinesia is presented. However, this movement disorder differed from classical tardive dyskinesia both in the nature of specific symptoms and in their relationship to neuroleptic treatment. Closer examination revealed evidence of neurological disorder preceding the earliest neuroleptic treatment. Although the nature of this disorder remains unclear, serious doubt exists whether it properly deserved a diagnosis of tardive dyskinesia, which opened the way for medicolegal dispute. The numerous ramifications of tardive dyskinesia speak for restrictive use of this diagnosis and for clear diagnostic criteria. 9 references. (Author abstract modified)

004781 Williamson, J.; Chopin, Joan M. University Dept. of Geriatric Medicine, City Hospital, Greenbank Drive, Edinburgh EH10 5SB, Scotland **Adverse reactions to prescribed drugs in the elderly: a multicentre investigation.** Age and Ageing. 9(2):73-80, 1980.

Prescribed drugs, patterns of prescription, and adverse drug reactions were surveyed in 1998 elderly patients consecutively admitted to 42 geriatric medicine departments in Great Britain in 1975 and 1976. Adverse reactions were noted in 248 patients, 15.3% of prescribed drug takers. In 209 of these patients, it was thought that an adverse reaction had contributed to the need for hospital admission. Full recovery from adverse reactions and sequelae occurred in 68% of those with reactions. Hypotensive drugs, antiparkinsonian drugs, and psychotropics carried the greatest risk of adverse reactions although the largest single number of adverse reactions were due to diuretics, the most commonly prescribed drugs (37.4%). Factors predisposing the elderly to adverse drug reactions are discussed, and the need for greater care in prescribing and supervising drugs in older patients is emphasized. 13 references. (Author abstract modified)

004782 Windorfer, A.; Pringsheim, W. Kinderklinik und Poliklinik der Techn. Univ. Munchen, Kolner Platz 1, D-8000 Munich, Germany **/Investigations on the influence of a tocolytic treatment of pregnant women with diazepam and fenoterol on the bilirubin levels and apgar score of the newborn./** Untersuchungen uber den Einfluss einer tokolytischen Behandlung schwangerer Frauen mit Diazepam und Fenoterol auf die Bilirubinkonzentration und Apgarwerte von Neugeborenen. Klinische Padiatrie. 191(1):51-60, 1979.

In a retrospective study of 2,618 pregnant women, the influence of diazepam monotherapy as well as the combination of diazepam and fenoterol on the bilirubin concentrations and Apgar scores of the newborn children was investigated. In the diazepam treated group 17% to 27% of the newborns showed Apgar scores of six or less. In the group treated with diazepam and fenoterol 66% to 68% of the newborn had Apgar scores of six or less. The effect of diazepam on the bilirubin levels appeared to depend on the dose and duration of the diazepam treatment. Following the combination therapy of diazepam and fenoterol, a significant number of the infants developed neonatal jaundice. It is concluded that the greater frequency of the low Apgar values and the larger bilirubin increase was possibly due to the higher diazepam concentration caused by fenoterol. 14 references. (Journal abstract modified)

004783 Woodhead, Richard. Division of Medicine, Bradford Royal Infirmary, West Yorkshire, England **Cardiac rhythm in tricyclic antidepressant poisoning.** Clinical Toxicology. 14(5):499-505, 1979.

One hundred adult patients with tricyclic antidepressant poisoning were studied by clinical observation and EKG monitoring. Sinus tachycardia was common, but dysrhythmias were not. EKG monitoring did not influence the treatment of these patients, suggesting that routine EKG monitoring may be unnecessary in cases of tricyclic antidepressant poisoning. 16 references. (Author abstract modified)

004784 Woodson, R. H.; da Costa-Woodson, E. M. Dept. of Growth and Development, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, England **Covariates of analgesia in a clinical sample and their effect on the relationship between analgesia and infant behavior.** Infant Behavior and Development. 3(3):205-213, 1980.

The effects of covariates of obstetric analgesia on the analgesia/infant behavior relationship were investigated in 113 Malay, Chinese, and Tamil Indian infants in a clinical Malaysian sample. Covariates examined included a variety of maternal, labor, and infant characteristics. Women administered obstetric analgesia were younger, of lower parity, underwent longer first and

second stages of labor, developed higher blood pressure, and were most likely to be Tamil and least likely to be Malay. Infant characteristics did not significantly vary as a function of analgesia administration. Parity, ethnic group, and duration of second stage of labor influenced the relationship between analgesia and infant irritability (but not alertness) on the Brazelton scale. When their effects were controlled, analgesia was found to be associated with decreased irritability. The combined influence of other maternal, labor, and infant variables, however, was comparable to that of analgesia. These findings illustrate the need to consider covariate effects in studies of obstetric analgesia. The relationship of maternal stress and distress during labor and cultural attitudes to decisions to administer analgesic medication is also discuseed. 17 references. (Author abstract modified)

16 METHODS DEVELOPMENT

004785 Bloom, Floyd E. Arthur V. Davis Center for Behavioral Neurobiology, Salk Institute, La Jolla, CA **The leading edge and beyond: future strategies for receptor mechanism research.** Psychopharmacology Bulletin. 16(3):94-95, 1980.

A cellular neuropharmacologist describes three important areas for future receptor mechanism research: 1) in vivo cellular studies; 2) in vitro cellular studies; and 3) molecular studies. Electrophysiological studies on the intact nervous system are judged to offer the most direct approach to receptor sensitivity changes but have the disadvantages of complexity and slowness. Novel receptor evaluation systems based upon measurement of activated glycogenolysis and functional ion flux response are cited. Receptor structure determinations by monoclonal antibodies and identification of new possible endogenous ligands developed through receptor predictions by recombinant DNA techniques are identified as technical advances of great promise. 7 references.

004786 Burch, W. M.; Butlin, A. T. Royal Canberra Hospital, Acton, A.C.T., 2601, Australia **A microcomputer-based simultaneous vigilance test.** Perceptual and Motor Skills. 50(3, Part 2):1195-1202, 1980.

A microcomputer based simultaneous vigilance test designed to examine the effects of anticonvulsants in epileptic patients is discussed. The use of microcomputer technology offers flexibility in development of a protocol and massive capability for data capture which cannot be equalled. The test period required to obtain an estimate of information processing rate is approximately 20 minutes. During this time data on reaction times, relationship between score and pattern symmetry, and the temporal sequencing of errors can be collected and stored in a readily analyzable form. 5 references. (Author abstract modified)

004787 Castro, Albert; Chung, Alfred; Monji, Nobuo. Dept. of Pathology (R40), University of Miami, School of Medicine, Miami, FL 33101 **Phenobarbital specific antibody production: preparation of 5-phenyl-5-(4-aminobutyl)barbituric acid-bovine serum albumin conjugate.** Research Communications in Chemical Pathology and Pharmacology. 28(2):309-317, 1980.

The aminobutyl derivative of phenobarbital, 5-phenyl-5-(4-aminobutyl)barbituric acid hydrochloride, was synthesized through two synthetic pathways for the preparation of immunogen in production of phenobarbital specific antibody. The antiserum had high titer, specificity, affinity, and sensitivity (0.5ng/ml) when examined by radioimmunoassay. 7 references. (Author abstract)

004788 Chase, T. N.; Neophytides, A.; Samuel, D.; Sedvall, G.; Swahn, C. -G. Experimental Therapeutics Branch, NINCDS, Bethesda, MD 20014 **Oxygen-18 use for clinical studies of central monoamine metabolism.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1569-1571).

The stable oxygen atom 18-02 was used to study central monoamine metabolism in six patients with Huntington's disease and four with Parkinson's disease. Inhalation of a mixture containing 18-02 for 1 hour resulted in measurable labeling of major monoamine metabolites in urine and spinal fluid. The time course for the appearance of 18-02 labeled metabolites suggested a relatively rapid turnover of the precursor central amines. Significant differences in the labeling and concentrations of homovanillic acid between the two patient groups suggest that patients with Parkinson's disease have a smaller dopamine pool with more rapid turnover than do patients with Huntington's disease. No toxicity due to 18-02 was observed in any patient. Results indicate that 18-02 can be used safely for acute biochemical studies related to oxidative metabolism in humans. 11 references. (Author abstract modified)

004789 Cohen, Bruce M.; Lipinski, Joseph F.; Pope, Harrison G., Jr. Mailman Research Center, McLean Hospital, Belmont, MA **Radioreceptor assays for neuroleptic drugs and clinical research in psychiatry.** Psychopharmacology Bulletin. 16(3):82-84, 1980.

The sensitivity of radioreceptor assays for neuroleptic drugs (NRRA) to neuroleptic activity in blood and tissue specimens of patients on a wide range of neuroleptic drugs, and the relationship between neuroleptic activity in blood and therapeutic effect were examined. A series of experiments demonstrate that the NRRA is able to detect neuroleptic activity in the blood of patients on a wide variety of neuroleptics. This ability may be of use in monitoring drug regimens and patient compliance. Each neuroleptic appears to produce a characteristic range of plasma neuroleptic activity, and thus, the therapeutic range must be individually determined for each drug. Plasma (and erythrocyte) neuroleptic activity appears to correlate well with therapeutic effect for patients receiving thioridazine in particular. The use of multiple radioreceptor assays and chemical assays together may be especially useful in studying individual drug metabolism and its relationship to clinical effects. 5 references.

004790 Coutts, R. T.; Baker, G. B.; Calverley, D. G. Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta, Canada T6G 2N8 **A rapid, sensitive method of measuring meta- and para-tyramine levels in urine using electron-capture gas chromatography.** Research Communications in Chemical Pathology and Pharmacology. 28(1):177-184, 1980.

A sensitive and inexpensive method for routine measurement of meta-tyramine and para-tyramine in small volumes of human urine is described. The procedure includes gas chromatography with electron capture detection. The detection limit for each amine is less than 20ng, and the procedure completely separates meta-tyramine and para-tyramine. 12 references. (Author abstract modified)

004791 Creel, Donnell. Veterans Administration Medical Center, Salt Lake City, UT 84148 **Inappropriate use of albino animals as models in research.** Pharmacology Biochemistry and Behavior. 12(6):969-977, 1980.

The inappropriate use of albino animals as normal models in biological research is reviewed and sensory/neural, biochemical metabolic, and physiological anomalies occurring in albino animals are discussed. All albino mammals examined have abnormal optic systems. Many drugs cannot be adequately evaluated in an albino S because of melanin's ability to bind and interact with some chemicals. There is evidence that a general reduction in melanin pigment is correlated with a paucity of amino acids

necessary for normal chemical function of the brain. There is a high probability that enzyme levels indicative of metabolic performance are deficient in the liver and kidneys of albinos. Congenital defects are associated with hypopigmentation in animal models and human syndromes. Melanin is found in abundance in the eye, inner ear, and midbrain where neural impulses are initiated, indicating a possible role as an electrophysiologic mechanism. Microwave irradiation differentially affects albino and pigmented animals. Implications of these observations and other reports of anomalies associated with hypopigmentation suggest caution in the use of albino and other hypomelanotic animals as normal models in biological research. 133 references. (Author abstract modified)

004792 Dencker, S. J.; Elgen, K. Dept. II, Lillhagen Hospital, Box 3005, S-422 03 Hisings Baack 3, Sweden **Aspects of clinical psychiatric research on depot neuroleptics. The presentation of two double-blind trials with cis(Z)-clopenthixol decanoate and a withdrawal study in schizophrenics.** Acta Psychiatrica Scandinavica. 61(Supplementum 279):5-9, 1980.

Methodological considerations in clinical psychiatric research on depot neuroleptics are discussed with reference to a series of studies of cis(Z)-clopenthixol decanoate in schizophrenic outpatients. Since such research is based primarily on clinical observations, elucidation of psychopharmacological effects must be based primarily on the assessment of symptoms/symptom cluster, side-effects, and global status. This requires rating scales that clearly define degrees of severity and are sensitive to minor changes. It is also necessary that changes in symptom profile be examined in conjuction with pharmacokinetic data; and that appropriate data recording formats be utilized. Scientific and practical/ethical requirements must be weighed to produce reliable and clear conclusions. Finally, it is important that observation periods be adequate: a period of three to five times the half-life of a drug is needed to obtain a steady rate, and the steady-state level probably needs to exist for some time before optimum effect on the receptor mechnaism can be assessed. These principles have been adhered to in a multicenter study involving two double-blind and a withdrawal investigation of cis(Z)-clopenthixol decanoate. 10 references.

004793 Free, Spencer M., Jr. Smith Kline and French Laboratories, Philadelphia, PA **Sample size in clinical drug trials -- discussion.** Psychopharmacology Bulletin. 16(2):48, 1980.

A paper on the problems associated with assuring an adequate sample size for clinical psychopharmacology research is critically evaluated, and an alternative procedure for assuring adequate sample size is offered. If one anticipates a multiple regression model analysis of the most appropriate factor score in a physician rating scale, a reasonable rule of thumb for defining sample size is to use two thirds of its value needed for binomial data with the desired Type I and Type II error considerations. It is noted that there are typically large treatment differences associated with drug vs. placebo studies in hospitalized patients, moderately large differences with drug vs. placebo studies in hospitalized patients, moderately large differences with drug vs. placebo studies in outpatients, and small differences with drug vs. drug comparison in inpatients.

004794 Goggans, Frederick C. Dept. of Psychiatry and Behavioral Sciences, Stanford University Medical Center, TD 114, Stanford, CA 94305 **Acute hyperkalemia during lithium treatment of manic illness.** American Journal of Psychiatry. 137(7):860-861, 1980.

A case report of a 67-year-old female patient who suddenly developed hyperkalemia during the treatment of acute manic illness with lithium is presented. The patient had acute hyperkalemia that was asymptomatic except for ECG abnormalities secondary to the hyperkalemia. It is noted that the differential diagnosis of acute hyperkalemia involves distinguishing pseudohyperkalemia, which is secondary to prolonged tourniquet time or hemolysis before potassium measurement, from true hyperkalemia. This distinction may be made by repeated potassium level determinations or by demonstrations of ECG changes consistent with hyperkalemia. It is speculated that lithium may disturb the electrochemical equilibrium across the cell membrane as it enters the cell, and result in increased potassium conductance. A subsequent loss of potassium into the extracellular fluid may lead to hyperkalemia in some patients. 7 references.

004795 Gold, Philip; DeFraites, Emanuel; Zis, Athanasios P. Clinical Psychobiology Branch, NIMH, Bethesda, MD **The LH response to dopamine infusion: possible marker for a central dopaminergic function in psychiatric patients.** Psychopharmacology Bulletin. 16(2):36-38, 1980.

Luteinizing hormone (LH) and prolactin (PRL) responses to a sustained intravenous infusion of dopamine (DA) in control Ss and drug free patients with either schizophrenia or major affective illness are described and the utility of the LH response to dopamine infusion as a marker of central dopaminergic function in psychiatric patients is discussed. The finding that LH responses in both schizophrenic and affectively ill Ss differs from those of normal Ss, is compatible with data in experimental animals which suggest that dopaminergic regulation of LH occurs only within the CNS via inhibition of hypothalamic luteinizing hormone releasing hormone, while dopaminergic regulation of PRL secretion occurs both within the CNS and outside at the pituitary level. 9 references.

004796 Guy, William; Ragheb, M.; Wilson, William H. Tennessee Neuropsychiatric Institute, Vanderbilt University, Nashville, TN 37203 **Utility of videotape in establishing interrater reliability.** Psychopharmacology Bulletin. 16(3):71-74, 1980.

The utility of videotaped clinical interviews in evaluating interrater reliability in multicenter clinical trials was evaluated, and the use of specifically designed interview videotapes to reduce interrater reliability is discussed. Twenty three participants in two collaborative studies of antidepressants who were employed at five research centers viewed six interviews with patients selected for videotaping on the basis of research diagnostic criteria for depressive disorders. The Hamilton Anxiety Scale and the Clinical Global Impressions/Severity of Illness were rated by Ss at all centers; the Brief Psychiatric Rating Scale was completed by Ss at three centers. The two major sources of rater errors were violations of the time frame and the rating context.

004797 Hardesty, Anne S.; Burdock, Eugene I.; Gershon, Samuel. Dept. of Psychiatry, New York University School of Medicine, New York, NY **Selection of subjects for drug trials.** Psychopharmacology Bulletin. 16(2):39-43, 1980.

The development and validation of a procedure for selection of Ss for drug trials on the basis of item analysis of clinical profiles and items from the Structured Clinical Interview (SCI) are described. Three aspects of the study are: identification of characteristic profiles of schizophrenics and depressives; 2) item analysis of baseline profiles of schizophrenics and depressives from two multinational, multicenter collaborative studies; and 3) application of the criteria for discriminating schizophrenics from depressives as determined by the item analysis to a new multicenter, single protocol study of two antidepressants (trazodone and imipramine) vs. a placebo. 4 references.

004798 Innis, Robert B.; Snyder, Solomon H. Snyder: Dept. of Psychiatry, Johns Hopkins University School of Medicine, Bal-

timore, MD **Neuroleptic radioreceptor assay and evaluation of a tricyclic antidepressant assay using (3H)-imipramine.** Psychopharmacology Bulletin. 16(3):80-82, 1980.

The development and validation of a neuroleptic radioreceptor assay are described, and the utility of a tricyclic antidepressant assay using (3H)-imipramine is evaluated. The major finding of the neuroleptic radioreceptor study is that neuroleptic serum levels are significantly correlated with clinical response as monitored by the Present State Examination. By contrast, drug dosage did not predict clinical response. Moreover, dosage and blood levels of the neuroleptics were not significantly correlated. It is contended that a tricyclic antidepressant radioreceptor assay using (3H)-imipramine would probably not have the advantage of the neuroleptic radioreceptor assay to detect active metabolites in proportion to their therapeutic activities. From a technical standpoint, (3H)-quinuclidinyl benzylate is a better radioreceptor ligand than (3H)-imipramine because of its greater reproducibility of binding nd higher ratio of specific to nonspecific binding. 10 references.

004799 Kolakowska, T.; Gelder, M. G.; Orr, M. W. Dept. of Psychiatry, University of Oxford, Littlemore Hospital Research Unit, Littlemore Hospital, Oxford OX4 4XN, England **Drug-related and illness-related factors in the outcome of chlorpromazine treatment: testing a model.** Psychological Medicine. 10(2):335-343, 1980.

Patients who presented with acute psychoses and were treated with chlorpromazine were first divided into two groups with good (n=23) and poor (n=13) outcomes. These outcome groups differed little in their initial clinical features and showed no differences in two indices of dopamine receptor blockage (extrapyramidal symptoms and plasma prolactin concentrations). The group which improved was then subdivided on the basis of evidence of dopaminergic blockage into 15 patients who had improved and also showed antidopamine effects (responders) and eight who had improved but showed no antidopamine effects (remitters). The remainder were eventually classified as resistant to the effects of the drug. The group of remitters contained no patients with nuclear schizophrenia; the responders were mainly nuclear schizophrenics; and the resistant patients were schizophrenic or schizoaffective. The three groups defined in this way also differed in their subsequent clinical course. It is suggested that this scheme for dividing patients may be useful in clinical work and could also asssist research workers to identify the patients who can most appropriately be studied to determine mechanisms of drug action. 28 references. (Author abstract)

004800 LaBrosse, Elwood H. Department of Pathology, University of Maryland School of Medicine, Baltimore, MD 21201 **Turnover and excretion of VMA by normal volunteers and patients with neural crest tumors.** In: Usdin, E., Catecholamines: basic and clinical frontiers. Oxford, Pergamon, 1979. 947 p. Vol. 2. (p. 1646-1648).

The turnover and excretion of 3-methoxy-4-hydroxymandelic acid (VMA) was studied in three normal volunteers and six patients with neural crest tumors following i.v. injection of 7-3H-VMA. The urinary excretion of 3H-VMA was rapid, with a biological half-life of about 0.5 hour. Up to 13% of the 3H-label was excreted as 3H20, but the remainder of the 3H-VMA was excreted unchanged. These results indicate that the urinary excretion of VMA can be used as a dynamic indicator of synthesis and metabolism of its catecholamine precursors. 9 references. (Author abstract modified)

004801 Loullis, C. C.; Hingtgen, J. N.; Shea, P. A.; Aprison, M. H. Hingtgen: Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, IN 46223 **In vivo determination of endogenous biogenic amines in rat brain using HPLC and push-pull cannula.** Pharmacology Biochemistry and Behavior. 12(6):959-963, 1980.

The in vivo determination of a number of biogenic amines in the perfusate of freely moving rats using high performance liquid chromatography (HPLC) and push/pull cannula methods is described. In an initial study, the lateral hypothalamus (LH) was chronically implanted with a push/pull cannula and 15 min samples were collected and aliquots of 200 microliter were injected into the HPLC without any extraction or prepurification procedure. Simultaneous determination of the levels of 5-hydroxytryptophan (5-HTP), 5-hydroxytryptamine (5-HT), 5-hydroxyindoleacetic acid (5-HIAA), norepinephrine (NE) and dopamine in the perfusate was accomplished by means of HPLC with electrochemical detection. In another study, 50mg/kg D,L-5-HTP was injected subcutaneously into rats implanted with push/pull cannula and working on a variable interval schedule of reinforcement. Increases in 5-HTP, 5-HT, and 5-HIAA were measured during the period of behavioral depression following 5-HTP administration. It is noted that this technique could provide a useful tool in the assessment of neurochemical changes in brain during ongoing steady-state behaviors or during the disruption of behavior following administration of drugs, precursors, or other perturbations. 19 references. (Author abstract modified)

004802 Lundberg, Paula K. Dept. of Psychology, University of Cincinnati, Cincinnati, OH 45221 **Assessment of drugs' side effects: visual analogue scale versus check-list format.** Perceptual and Motor Skills. 50(3, Part 2):1067-1073, 1980.

The sedative effects of two antihistamines, diphenhydramine and terfenadine, were measured by two different instruments on 12 subjects. By employing two different assessments of side-effects it was possible to compare the sensitivities of a checklist format and a visual analogue scale format for the detection of side effects. Results suggest that subjects are capable of perceiving and reliably reporting the ongoing flow of their bodily experiences. For the measurement of side-effects, an instrument which employs a visual analogue scale may be a more sensitive measure device than a typical checklist format. 6 references.

004803 Metys, J.; Dlabac, A. Kourimska 17, 130 00 Prague 3, Czechoslovakia **Action of psychotropic drugs on behavioural syndrome induced by 5-hydroxytryptophan in rats.** Activitas Nervosa Superior. 22(2):94-95, 1980.

The influence of a series of neuroloeptic drugs, trycyclic antidepressants, and new antimigraine drugs on the behavioral syndrome induced by 5-hydroxytryptophan (5-HTP) in rats was investigated. The 5-HTP induced behavioral syndrome consists of resting tremor, rigidity, rhythmic, dorsoventral movements of the forelimbs, hindlimb adbuction, Straub tail, and lateral head weaving. Neuroleptic drugs with pronounced central antidopaminergic activity were compared. Tricyclic antidepressants under investigation showed substantially lower inhibitory activity against 5-HTP induced syndrome in rats. It is concluded that the 5-HTP behavioral syndrome represents a useful tool for evaluating effects of psychotropic drugs in CNS serotonin. 6 references.

004804 Neuvonen, P. J.; Elonen, E. Dept. of Clinical Pharmacology, University of Helsinki, Paasikivenkatu 4, SF-00250 Helsinki 25, Finland **Effect of activated charcoal on absorption and elimination of phenobarbitone, carbamazepine and phenylbutazone in man.** European Journal of Clinical Pharmacology. 17(1):51-57, 1980.

The effect of activated charcoal, given as a water suspension on the absorption and elimination of phenobarbitone, carbama-

zepine, and phenylbutazone was studied in five healthy volunteers, using a randomized crossover design. Absorption of the drugs was almost completely prevented when charcoal was ingested within 5 min of taking the drugs. Although activated charcoal should be given as soon as possible, even its delayed use may be indicated, due to the slow absorption often seen in acute intoxication. The use of multiple doses of charcoal appears to be indicated as an additional treatment of certain severe intoxications to prevent the release of drugs from charcoal, and to increase their rate of elimination if they are secreted into the gut with subsequent reabsorption. 23 references. (Author abstract modified)

004805 Overall, John E. University of Texas Medical School, Houston, TX **Sample size in clinical drug trials.** Psychopharmacology Bulletin. 16(2):46-48, 1980.

Statistical methodology in clinical psychopharmacology research is discussed in relation to various procedures for determining the sample size required to provide adequate power for detecting true treatment differences. Practical considerations underlying the current practice of clinical drug trials with insufficient sample size are identified. It is argued that conventions should be adopted for defining meaningful treatment differences in clinical psychopharmacology research similar to the convention of the .05 level of confidence (statistical significance). It is suggested that treatment effects be stated in terms of the proportion of times, the (imperfectly) measured response to treatment A should be expected to be superior to that of treatment B in matched pairs of Ss. By adopting this convention, the question of appropriate sample size would be completely determined, with no additional estimates required.

004806 Papadopoulos, Andreas S.; Chand, T. G.; Crammer, J. L.; Lader, Susan. Crammer: Institute of Psychiatry, London, S.E.5, England **A pilot study of plasma thioridazine and metabolites in chronically treated patients.** British Journal of Psychiatry. 136:591-596, 1980.

Plasma concentrations of thioridazine, mesoridazine, sulphoridazine, and thiofidazine ring sulphoxide were measured individually by specific gas liquid chromatographic (GLC) methods and collectively by a radio receptor assay in 16 elderly inpatients during chronic treatment. The sulphoridazine level was above 0.135mcg/ml in five out of six symptomatically well controlled Ss and was below this level in 9 out of 10 Ss who were poorly controlled. No such division was so clear for the other substances measured. A new assay for the total dopamine receptor-blocking activity of the plasma correlated highly at lower levels with the sum of drug plus metabolites obtained by GLC, but exceeded the sum at higher values. Both sulphoridazine and neuroleptic levels need further study. 12 references. (Author abstract)

004807 Popkin, Michael K.; MacKenzie, Thomas B.; Hall, Richard C. W.; Callies, Allan L. Box 345, Mayo Building, University of Minnesota Hospitals, Minneapolis, MN 55455 **Consultees' concordance with consultants' psychotropic drug recommendations: related variables.** Archives of General Psychiatry. 37(9):1017-1021, 1980.

To identify variables critical to consultees' concordance with the recommendations of psychiatric consultants for the use of psychotropic medications in a general hospital, the medical records from 394 psychiatric consultations were reviewed. Seven variables were found to be significantly related to concordance. Among these were the patient's history of exposure to psychotropic medications, the presence of multiple recommendations, specification of starting dosage, the category of psychotropic drug recommendation, and the timing of the consultation. The latter two variables emerged as most noteworthy. This work extends the investigation of consultees' responses to consultants' recommendations and anticipates the development of specific consultation strategies derived from quantitative outcome studies. 2 references. (Author abstract modified)

004808 Rosenblatt, Jack E.; Pary, Robert J.; Bigelow, Llewellyn B. Lab of Clinical Psychopharmacology, NIMH, St. Elizabeths Hospital, Washington, DC **Measurement of serum neuroleptic concentrations by radioreceptor assay: concurrent assessment of clinical response and toxicity.** Psychopharmacology Bulletin. 16(3):78-80, 1980.

A sensitive radioreceptor assay for neuroleptic drugs in serum was used to examine the relationship between serum neuroleptic concentration and clinical response. The radioreceptor assay was found to be highly reliable. Its validity is suggested by close correlation of serum haloperidol concentration measured by both radioreceptor assay and radioimmunoassay. However, higher values were obtained with the radioreceptor assay, suggesting the possible presence of active haloperidol metabolites. The use of this radioreceptor assay with several patient and S groups in relation to side-effects and symptomatic relief of neuroleptics is briefly described. 5 references.

004809 Rubin, Robert T.; Forsman, Anders; Heykants, Jos; Ohman, Rolf; Tower, Barbara; Michiels, Marcel. B-4 Neuroendocrine Laboratory, Harbor/UCLA Medical Center, Torrance, CA 90509 **Serum haloperidol determinations in psychiatric patients: comparison of methods and correlation with serum prolactin level.** Archives of General Psychiatry. 37(9):1069-1074, 1980.

Twenty one serum samples from 11 schizophrenic patients receiving long-term haloperidol therapy were analyzed for haloperidol concentrations by two different radioimmunoassays (RIAs) and gas chromatography (GC). There was a good correspondence between the RIA and GC values over a wide range of drug concentrations. However, compared with the specific GC technique, both RIA methods overestimated haloperidol concentrations, reflecting differences in the specificities of the two RIA antibodies. One of the RIA methods had the requisite specificity for application to patients treated with long-term haloperidol therapy, although further methodological refinement will be required for its general clinical application. Haloperidol values determined by GC and RIA analyses correlated highly with prolactin concentrations in the same samples, suggesting that the usefulness of prolactin measurement as an in vivo bioassay for circulating levels of haloperidol should be further explored. 43 references. (Author abstract)

004810 Rubin, Robert T.; Hays, Sally E. Dept. of Psychiatry, Harbor/UCLA Medical Center, Torrance, CA 90509 **The prolactin secretory response to neuroleptic drugs: mechanisms, applications and limitations.** Psychoneuroendocrinology. 5(2):121-137, 1980.

The mechanisms, clinical applications, and limitations to these applications of the prolactin (PRL) secretory response to neuroleptic drugs are reviewed. Although measurement of increased serum PRL has been proposed as in vivo bioassay in psychiatric patients for the concentration of neuroleptic binding to anterior pituitary lactotroph dopamine (DA) receptors, the clinical applicability of this hormone test involves several difficulties. One difficulty is the extreme sensitivity of the lactotroph DA receptors, such that clinically effective neuroleptic doses may stimulate PRL secretion maximally, thereby necessitating subclinical low dose paradigms for establishing drug dose PRL response curves. Another difficulty is the large interindividual variability in PRL secretion profiles, even in normal nonpsychotic volunteers giving neuroleptics intravenously. Thus, for comparative

purposes, extended serial blood sampling protocols must be conducted over several hours to fully characterize PRL secretion profiles. Additionally, the effect of a neuroleptic drug at the pituitary lactotroph may not reflect its antipsychotic effect in the CNS. Also, neuroleptics developed in the future may not work primarily by DA receptor blockade. 67 references (Author abstract modified)

004811 Sanberg, Paul R.; Pisa, Michele; Faulks, Ian J.; Fibiger, Hans C. Dept. of Behavioural Biology, Research School of Biological Sciences, Australian National University, Canberra City, A.C.T. 2601, Australia **Experiential influences on catalepsy.** Psychopharmacology. 69(2):225-226, 1980.

The effects of experience in a standard catalepsy test on catalepsy ratings in that test were investigated in male Wistar rats. With repeated testing the animals showed a progressive increase in their catalepsy scores. It is suggested that this behavior may be a form of tonic immobility, and is not due to the repeated saline injection, since similar results are obtained with uninjection animals. Therefore, pharmacological investigations of catalepsy must include drug injected and control animals matched for experience, as well as for the usual factors. 13 references. (Author abstract modified)

004812 Schooler, Nina R. NIMH, Rockville, MD **How generalizable are the results of clinical trials?** Psychopharmacology Bulletin. 16(3):29-31, 1980.

Issues concerning the generalizability of results of clinical drug trials and possible nonrandomness of S characteristics among clinical drug trials are discussed. It is noted that an ideal clinical trial in psychopharmacology should be conducted in the context of population based information, so that the relationship of the study sample to a real population of interest can be specified. While such studies may be possible in the future, they are not routinely possible at present. Therefore, researchers must be content to: 1) provide information about excluded cases; (2) design studies with hypotheses about nature of effects excluded cases could have, and if possible, test these; and 3) be specific in reporting results about to whom results can be generalized and provide readers sufficient information about excluded Ss so they can agree or disagree. 5 references.

004813 Silverman, G. St. Bernard's Wing, Ealing Hospital, Southall, Middlesex, England **Placebo effect and changes in response set with re-testing: a further source of bias.** Neuropharmacology. 18(12):1019-1021, 1979.

In a study of the effect of retesting on response set, 10 Ss rated eight photographs from the Grid Test for Schizophrenic Thought Disorders on four occasions separated by weekly intervals. Results of three experiments showed that scores tended to move consistently toward a midpoint upon retesting. This effect, named the Heracleitean effect, may contribute to the placebo response and to spurious drug effects in psychopharmacological testing. 9 references.

004814 Taeuber, Karl; Appel, Eva; Badian, Mario. Medical Dept., Hoechst, AG, Frankfurt/Main, Germany **The delayed auditory feedback (DAF) method for inducing stress in experiments with beta-blockers and benzodiazepines.** Psychopharmacology Bulletin. 16(3):74-75, 1980.

The development and validation of the delayed auditory feedback (DAF) method for inducing stress in experiments with beta-blockers and benzodiazepines are described. Both the electrodermal and cardiovascular changes induced at baseline are extremely constant, indicating good reproducibility of the DAF model. Apparently both classes of drugs are active against different activation mechanisms which occur as responses to stress. The beta-blockers reduced only the tachycardiac response to the DAF procedure, whereas diazepam and, less clearly, clobazam reduced the electrodermal responses which are regarded as being indicators of CNS arousal. 5 references.

004815 Tyler, Thomas D.; Tessel, Richard E. Tessel: Dept. of Pharmacology and Toxicology, School of Pharmacy, University of Kansas, Lawrence, KS 66045 **A new device for the simultaneous measurement of locomotor and stereotypic frequency in mice.** Psychopharmacology. 64(3):285-290, 1979.

The utility of a new apparatus in measuring simultaneously and objectively both locomotor activity and stereotypy induced in individual mice by d-amphetamine, morphine, cocaine, and methylphenidate was comparatively evaluated with commonly used visual observational scoring procedures. The basis for the differential quantifying capacity of the appparatus resides in two capacitive sensors which respond to animal induced changes of a tuned resonating capacitive field. The responses of the capacitive sensors produce voltage pulses proportional to the amplitude of eninal movements. These pulses are then counted. sensitivity measurement (total counts) recorded such movements as licking and grooming as well as movements of greater body mass (locomotion). Respiration was not recorded. Low sensitivity measurement (locomotor counts) recorded only movements of relatively greater body mass such as locomotion and rearing onto hind legs. Stereotypic activity was defined as total counts less locomotor counts. Changes induced by cocaine, methylphenidate, and morphine in locomotor and stereotyped behaviors measured electronically agreed closely with the results of the observational scoring procedures. When measured by machine, the d-amphetamine dose/response data also compared well with the observational results, except at the highest dose (32mg/kg). This dose of d-amphetamine induced extreme stereotypy of sufficient amplitude to be recorded as locomotor activity by the apparatus. The results indicate that the expanded behavioral measurement capabilities of this apparatus offer several advantages over previous related measurement techniques. 17 references. (Author abstract modified)

004816 Wood, James H. Div. of Neurosurgery, Hospital of the University of Pennsylvania, 3400 Spruce St., Philadelphia, PA 19104 **Neurochemical analysis of cerebrospinal fluid.** Neurology. 30(6):645-651, 1980.

The use of cerebrospinal fluid (CSF) analysis for studying in vivo alterations in central neuronal activity is discussed. Ventriculospinal concentration gradients, circadian rhythms, physical activity, stress, medications, precursor intake, illness, obstructed CSF circulation, age, and sex alter the baseline neurochemical composition of CSF. Differential probenecid blockade of the egress of acidic monoamine metabolites and cyclic nucleotides from the CSF may complicate interpretations of their accumulations. Degradation of CSF constituents during collecton, storage, and analysis may introduce errors in quantification. These sources of CSF variability can be minimized with proper methodology. 84 references. (Author abstract)

17 MISCELLANEOUS

004817 Abramson, Ronald; Garg, Mithlesh; Cioffari, Arletta; Rotman, Phyllis A. 13 Pelham Island Road, Wayland, MA 01778 **An evaluation of behavioral techniques reinforced with an anorectic drug in a double-blind weight loss study.** Journal of Clinical Psychiatry. 41(7):234-237, 1980.

Sixty obese outpatients participated in a double-blind comparison of diethlpropion hydrochloride (an anoretic drug) and placebo in conjunction with a behavior modification program for weight reduction. Assessments of efficacy and program acceptance included total weight loss, percent of initial (baseline) weight loss, percent excess weight loss, effectiveness of overall program, and helpfulness of medication. Diethylpropion was significantly better than placebo in all five assessments. An added behavioral technique, a substantial refundable deposit of money, reduced the attrition rate of all study entrants from 50% to 10%; thus patient compliance was greatly enhanced. 14 references. (Author abstract)

004818 Alpert, Murray; Friedhoff, Arnold J. Dept. of Psychiatry, New York University Medical Center, 550 First Avenue, New York, NY 10016 **An un-dopamine hypothesis of schizophrenia.** Schizophrenia Bulletin. 6(3):387-390, 1980.

The dopamine hypothesis of schizophrenia is examined critically. The three main bases of the hypothesis are: 1) pharmacotherapy of schizophrenia appears to require reduction in CNS dopaminergic activity with a rough proportionality between the amount of drug used clinically and its in vitro potency at the dompamine/neuroleptic receptor; 2) schizophrenics appear to be especially sensitive to drugs which increase CNS dopaminergic outflow; and 3) intensive and extensive exposure to amphetamines produces a psychosis in nonschizophrenics which is strikingly similar to paranoid schizophrenia. Thus, supporting evidence is largely pharmacological. Further, neuroleptic mechanisms do not fit a simple hyperdopaminergic formulation, and treatment efficacy points to a general psychotic rather than specific schizophrenic role for dopamine. Most compromising to the hypothesis is the therapeutic action of L-dopa when combined with neuroleptics in chronic schizophrenics. Dopamine appears important, but cannot be viewed as a simple pathogen. 23 references. (Author abstract modified)

004819 Amdur, Mark A. Dept. of Psychiatry, Northwestern University, School of Medicine, Chicago, IL 60611 **Medication compliance in outpatient psychiatry.** Comprehensive Psychiatry. 20(4):339-346, 1979.

An outline of factors relating to compliance among psychiatric outpatients is presented. These factors are organized into three areas: features of the therapeutic regimen; features of the patient; and features of the physician. Regarding the therapeutic regimen, it is suggested that the medication regimen should not conflict with existing daily habits and that complex schedules for taking medication should be avoided. A major patient related consideration is the greater likelihood to take medication when troubled by immediate distress; where the causal relationship between drug taking and symptom relief is more apparent. Physicians should note that shared values and an empathic, nonjudgmental approach enhance compliance, and that manifest enthusiasm toward treatment will be directly related to treatment success. 14 references.

004820 Amsterdam, J. D.; Brunswick, D. J.; Mendels, J. Depression Research Unit (151-E), V.A. Hospital, University and Woodland Avenues, Philadelphia, PA 19104 **Reliability of commercially available tricyclic antidepressant levels.** Journal of Clinical Psychiatry. 41(6):206-207, 1980.

Results of tests of plasma levels of tricyclic antidepressants from four laboratories were compared using identical plasma samples containing amitriptyline and nortriptyline in order to assess interlaboratory reliability. Good agreement was generally found between investigators' results and those of commercial facilities; however, some large interlaboratory discrepancies were evident. Caution is advised when utilizing plasma tricyclic levels to monitor patient progress. Use of a laboratory well established in this area is suggested. 7 references. (Author abstract modified)

004821 Andrysiak, Therese; Carroll, RoseMary; Ungerleider, J. Thomas. THC-Ohcology research project, Neuropsychiatric Institute, University of California, Los Angeles, CA **Marijuana for the oncology patient.** American Journal of Nursing. 79(8):1396-1398, 1979.

An ongoing study comparing the relative efficacy of marijuana and prochlorperazine (Compazine) for relieving the negative side-effects of chemotherapy for cancer patients is reported. Compazine and marijuana were given to 115 patients in a double-blind study. Possible physiological, psychological, psychosomatic and somatic effects that can occur from marijuana are described. Some interesting patient reactions are reported. Precautionary measures before giving a cancer patient marijuana are considered. No conclusive results have yet been obtained on marijuana's effectiveness in alleviating loss of appetite, nausea, and vomiting caused by chemotherapy. 6 references.

004822 Ariens, E. J. Institute of Pharmacology and Toxicology, University of Nijmegen, Geert Grooteplein N21 P.O. Box 9101, 6500HB Nijmegen, The Netherlands **Receptors: from fiction to fact.** Trends in Pharmacological Sciences. 1(1):11-15, 1979.

The development and current status of the receptor concept in pharmacology are reviewed. It is noted that the receptor concept has been indispensable for discussing and understanding the mode of action of pharmacy for several decades. With the mass action law as a basis, various receptor theories and models have been formulated to interpret the dose/response and dose/binding curves observed. With the possibility of receptor localization, identification, and isolation, the use of receptor binding studies as a screening method in the development of new bioactive agents and the development of receptor pathology, the receptor concept has been converted to operational reality. Topics discussed include: affinity and intrinsic activity; occupation activation model; amplifier system and spare receptors; complementarity postulate; two state model; mobile receptor hypothesis; and three ligand concept. 21 references. (Author abstract modified)

004823 Avrutskaya, I. G. Otdel oligofrenii Moskovskogo NII psikhiatrii MZ RSFSR, Moscow, USSR /**The selective action of metabolic drug therapy in mentally deficient children.**/ Ob izbiratel'nosti deystviya preparatov metabolicheskoy terapii u detey s intellektual'noy nedostatochnost'yu. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(3):436-439, 1980.

Metabolic drug therapy for mentally deficient children was studied with particular emphasis on aminalon, piriditol, pantogam and piracetam. The Ss were children suffering from mental retardation, borderline conditions of mental deficiency, and severe oligophrenia. These conditions were complicated by dif-

ferent psychopathic states, namely: torpidity, motor excitation, psychopathic syndrome, and cerebral deficiency syndrome. Results show that the drugs which were used appear to be the most effective in treating mental retardation. 8 references (Journal abstract modified)

004824 Bakalar, James B. 74 Fenwood Road, Boston, MA 02115 **Psychedelic drug therapy: cultural conditions and obstacles.** Journal of Altered States of Consciousness. 5(4):297-307, 1980.

Cultural obstacles and conditions for psychedelic drug therapy are examined within the history of the rise and decline of the therapeutic use of such drugs as peyote and lysergic acid diethylamide (LSD) between the 1950s and the present. It has become almost impossible to use LSD and other psychedelic drugs in psychotherapy; and the reason is not simply doubt about their safety and efficacy. Rather, four issues are involved: the purpose of drug use in psychotherapy; the relation of psychotherapy to religious experience; the religious significant of drug use; and the social consequences of certain kinds of religious experience. Modern attitudes toward these problems make mistrust and disapproval of the therapeutic use of psychedelic drugs inevitable. Alternative attitudes are suggested; and it is concluded that if it is admitted that psychedelic substances are not drugs by any of the narrow definitions now institutionally established and legally enforced, then it may become possible to distinguish rational from irrational fears and make an appropriately limited use of psychedelics for therapeutic, religious, and other purposes. 5 references. (Author abstract modified)

004825 Bambrick, James R. University of Windsor (Canada) **Effect of two levels of methylphenidate hydrochloride for hyperkinetic children on measures of attention and mother-child interaction. (Ph.D. dissertation).** Dissertation Abstracts International. 40(4):1876-B, 1979. (Not available from Univ. Microfilms), 1979.

Dose response relationships and social and attention behaviors of hyperkinetic children were examined. Twelve hyperactive boys, 7 to 12 years old, were observed under three medication conditions: placebo, Ritalin 0.3mg/kg, and Ritalin 1.0mg/kg. No main effects for medication were noted for scores on an attention task, nor was medication level observed to exert an influence on any of the categories of mother-child interaction. However, for both sets of variables, active medication conditions were observed to optimally enhance the performance of greater numbers of subjects than placebo. The observation of wide intersubject variation in optimal dosage levels of medication called into question the universality of dose response relationships across samples of subjects. It is suggested that an individual's response to medication may vary considerably from group dose response relationships for specific target behaviors. (Journal abstract modified)

004826 Berendes, Margret. 4300 Fordham Road, Washington, DC 20016 **Formation of typical, dynamic stages in psychotherapy before and after psychodelic drug intervention.** Journal of Altered States of Consciousness. 5(4):325-338, 1980.

Observations made on 12 patients during their psychoanalytically oriented psychotherapy, before and after they underwent psychedelic drug interventions, are reported. The anticipated event had a remarkable impact on therapy, manifested by acceleration as well as intensification and a typical development of two major psychodynamic stages before the intervention and an unexpected gentle resolution of transference and tendency for termination of the treatment by the patient afterwards. To different conceptual models, the classical psychoanalytical Freudian concept and Grof's much more extended framework with a different resulting approach, are applied to explain the major effect of the unspecific drug induced deep regression and final development of therapy. 11 references. (Author abstract)

004827 Buckholtz, Neil S. Dept. of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC 29403 **Neurobiology of tetrahydro-beta-carbolines.** Life Sciences. 27(11):893-903, 1980.

Neurochemical, neuroendocrinological, and behavioral effects of tetrahydro-beta-carbolines (THBCs) are reviewed. In vitro and in vivo studies have shown that these tricyclic compounds, which are structurally related to indoleamines, formed endogenously in brain and other tissues. They appear to interact relatively specifically with serotonergic mechanisms and may serve as endogenous neuromodulators or neurotransmitters. 80 references. (Author abstract modified)

004828 Cain, Nancy N.; Cain, Russell M. University of Rochester Community Mental Health Center, Rochester, NY 14642 **A compendium of antidepressants.** Clinical Toxicology. 14(5):545-574, 1979.

A compendium of available tricyclic antidepressants, monoamine oxidase inhibitors, lithium carbonate, and stimulants is presented. The charts include adult dosages, drug precautions, side-effects, interactions with other drugs, and effects on clinical laboratory tests. Basic information on the prevention and management of overdoses of these agents is also provided. 5 references. (Author abstract modified)

004829 Calne, Donald B. Building 10, Room 6D20, NINCDS, NIH, 9000 Rockville Pike, Bethesda, MD 20205 **Neurotransmitters, neuromodulators, and neurohormones.** Neurology. 29(11):1517-1521, 1979.

The merging of research in neurology and endocrinology is discussed. The role of neurotransmitters, which control membrane excitability by altering specific ion conductance, is compared to that of neuromodulators, which modify subsynaptic transmitter coupled mechanisms. Recent developments in peptide pharmacology are reviewed, with emphasis on the endorphins and enkephalins. 32 references.

004830 Cohen, Neal L. Dept. of Psychiatry, New York University School of Medicine, New York, NY 10003 **Integrating pharmacotherapy with psychotherapy: the consulting relationship.** Bulletin of the Menninger Clinic. 44(3):296-300, 1980.

The role of medication in analytic treatment is discussed. Common acceptance of the fact that genetic factors in manic-depressive illness and schizophrenia result in a deficiency in the development of ego functions allows many analytic practitioners to accept a role for drugs ancillary to psychoanalytic therapy. Low doses of neuroleptic drugs may also serve as part of the system" in the analytic treatment of some patients with borderline personality disorder, and in some therapeutic work with psychotic patients. Some guidelines for an optimal consulting relationship between an analytic clinician and a medicating psychiatrist are proposed. 8 references.

004831 Covi, Lino; Lipman, Ronald S.; McNair, Douglas M.; Czerlinsky, Thomas. Johns Hopkins Hospital, Henry Phipps Psychiatric Clinic, B.G., 601 North Broadway, Baltimore, MD 21205 **Symptomatic volunteer in multicenter drug trials.** Progress in Neuro-Psychopharmacology. 3(5/6):521-533, 1979.

The recruitment and use of symptomatic volunteers in multicenter trials of antianxiety and antidepressant drugs are discussed. Symptomatic volunteers were recruited at two collaborating institutions via advertisements placed for volunteers with significant symptoms of anxiety, depression, or both, and who were not currently in treatment. It was possible to recruit ade-

quate numbers of volunteers who met the numerous criteria, such as medical contraindications. Acceptable homogeneity across the samples at the collaborating institutions was found for demographic characteristics, level of distress, duration of symptoms, etc. Attrition rates for these volunteers were lower than for the typical anxiolytic and antidepressant trials using outpatients. Symptomatic volunteers appear to present a feasible alternative to the increasingly diminishing pool of outpatients. 18 references. (Author abstract modified)

004832 Dowling, J. T. Dept. of Cardiolo;gy, Royal Melbourne Hospital, Melbourne, Australia **Relief of anxiety and pain in cardiac patients.** Current Therapeutics 21(6):92-93, 95-96, 98-100, 103 1980.

The problem of managing pain and anxiety from myocardial ischemia is addressed. Useful drugs in treating cardiac patients are identified, along with approaches to controlling unstable angina. Indicators of the need for coronary artery surgery are presented, and the benefits of tranquilizers in preventing attacks of angina pectoris are evaluated. Effective management of symptoms is considered crucial since pain and anxiety can significantly alter lifestyle and general psychological well-being in cardiac patients.

004833 Feinstein, A. R. Yale University School of Medicine, New Haven, CT 06510 **Should placebo-controlled trials be abolished?** European Journal of Clinical Pharmacology. 17(1):1-4, 1980.

Ethical and methodological issues concerning the use of randomized, placebo controlled, drug trials are discussed. It is noted that in the attack on the merits of randomized, controlled, therapeutic trials, there is often confusion concerning the various components of clinical trials. These components are reviewed, and the use of placebo controlled trials is defended. Topics discussed include: concurrent and historical comparisons in controlled trials; the advantages of randomization in assigning treatments; limitations to randomized trials; the advantages of double-blind trials; the advantages of placebo rather than no treatment controls; excessive use of placebo trials; ethical issues concerning no treatment controls; and the need to develop better forms of nonrandomized evidence to evaluate therapy.

004834 Fischer, Roland. Port D'Es Canonge, Esporles, Mallorca, Spain **On the arousing effect of hallucinogens or who is who under psilocybin.** Journal of Altered States of Consciousness. 5(4):321+324, 1980.

Individual variation in response to hallucinogenic drugs such as LSD, mescaline, and psilocybin is discussed. The arousing effect of hallucinogens on limbic structures as well as on brain stem reticular formation depends on optimal sensory input. Minimizers or reducers of sensory input (i.e., subjects who display a large standard deviation on perceptual/behavioral tasks) and maximizers or augmenters of sensory input (who are stable subjects with a small standard deviation) prefer to adjust sensory input at drug peak to their higher and lower baselines of arousal. Hence, at hallucinogenic drug peak and in an environment of sensory attenuation, maximers, being unable to optimize (increase) sensory input, will not develop a hallucinatory experience. Minimizers, on the other hand, being already provided with an optimal (low) sensory input, will have a hallucinogenic experience. A psilocybin experience described by Robert Graves is quoted to exemplify the above observations and illustrate them. 10 references. (Author abstract modified)

004835 Foster, Richard Wathen. University of Chicago **Drugs and the changing politics of public mental hospitals.** Dissertation Abstracts International. 40(4):2161-A, 1979. (Not available from Univ. Microfilms), 1979.

Changes in public mental hospital utilization between 1955 and 1970 are explored using a theory based upon group interest politics which views the introduction of psychotropic drugs as disrupting the pre-1955 equilibrium by altering the structure of demand for patient release by various interest groups. Social workers and nursing homes were hypothesized to more strongly favor early patient release which would increase the demand for the services of the interest group. The bulk of mental hospital employees were hypothesized to resist efforts to shorten patient stays since their work is related to inpatient census. A series of cross-sectional regressions relating changes in patient stay to the political strength of the groups whose interests were altered was used to test this thesis. Alternative explanations for declining patient stay were examined, and it was shown that shorter stays have not decreased the tax burden and that new developments in psychopharmacology and changes in drug usage cannot by themselves explain the pattern of change. No relationship was found between length of stay and welfare program or private and outpatient treatment availability. States exhibiting the greatest reduction in length of hospitalization were not those previously identified as being relatively innovative across a broad range of government programs. Additional research refining measures of political strength and interest structure of the groups initially considered produced mixed results. (Journal abstract modified)

004836 Gerson, Cyrelle K. no address **Hospice: people-centered care.** American Pharmacy. NS20(6):27-29, 1980.

The hospice movement is discussed and the theory on the use of drugs in a hospice is considered. The hospice concept centers directly on the patient and family needs in a terminal illness. The focus is on pain control and palliative treatment. Areas of symptom control include pain and the anxiety that accompanies it, nausea and vomiting, constipation, diarrhea, anorexia, and drug side-effects. The use of nonnarcotic analegesics is recommended for initial stages and high doses of narcotics are required in later stages. Administrative and financial problems involved in drug use are noted. It is concluded that pharmacists can contribute to hospice care in the areas of administration, education, patient consultation, and public relations. 5 references.

004837 Greengard, Paul. Dept. of Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Some chemical aspects of neurotransmitter action.** Trends in Pharmacological Sciences. 1(1):27-29, 1979.

The current literature on the possible role of cyclic nucleotides and phosphorylated proteins as mediators of the actions of neurotransmitters and psychoactive drugs is briefly reviewed. It is noted that adenylate cyclases and guanylate cyalases appear to mediate certain actions of neurotransmitter in the brain. Similarities and differences between the cyclic AMP system and the cyclc GMP system are examined. Phosphorylated proteins as physiological effectors in the nervous system are discussed. 19 references.

004838 Grohmann, R.; Strauss, A.; Gehr, Ch.; Ruther, E.; Hippius, H. Ruther: Psychiatrische Klinik, Universitat Munchen, Nussbaumstrasse 7, D-8000 Munich 2, Germany /**The practice of clinical therapy with psychotropic drugs: retrospective investigation of physicians' prescribing practices in a psychiatric hospital.**/ Zur Praxis der klinischen Therapie mit Psychopharmaka: retrospektive Untersuchung der Verordnungsgewohnheiten in einer Psychiatrischen Universitatsklinik. Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(1):1-19, 1980.

Physicians' practices in prescribing psychotropic drugs at a German psychiatric hospital were investigated using data from

2100 patients. Data were obtained on the administration of the most popular drugs (clozapine, chloralhydrate, and amitriptyline), the use of single substances versus a combination of different drugs, and the mean time of combined drug treatment. Compounds with sedative effects were preferred within all classes of psychotropic drugs. It was evident that combinations of psychotropic drugs are widely used in clinical practice. This pattern of psychopharmacological drug treatment is in conflict with the presently accepted rule of pharmacotherapy. It was also surprising to find that single components of drug combinations are changed very often. 29 references. (Journal abstract modified)

004839 Houlihan, William J. no address **The chemistry of heterocyclic compounds. Volume 25. Indoles. Part 3.** New York, Wiley, 1979. 586 p. $70.00.

Two reviews on hydroxyindoles, indole alchols, and indolethiols and on indole aldehydes and ketones are presented. The indoles described are important as psychoactive agents, as structural components of physiologically active alkaloids, and as biologically active compounds in their own right. Syntheses, reactions, and properties of these compounds are described, and a table of hydroxyindole color reactions for use in thin layer chromatography is included. 1600 references.

004840 Jonas, O. Strathmont Centre, Grand Junction Road, Gilles Plains, South Australia 5086 **Pattern of drug prescribing in a residential centre for the intellectually handicapped.** Australian Journal of Developmental Disabilities. 6(1):25-29, 1980.

A survey of drug prescribing for retarded residents of a residential center in South Australia was undertaken to establish baseline data, which could subsequently be used to evaluate changes in the extent and pattern of drug use. Of the 596 residents, 513 were taking one or more of 155 drugs. Information is presented on the frequency and types of medications prescribed. (Author abstract modified)

004841 Knutsson, Evert. Dept. of Clinical Neurophysiology, Karolinska sjukhuset, Stockholm, Sweden **Antispastic medication.** Scandinavian Journal of Rehabilitation Medicine. Supplement No. 7:80-84, 1980.

The use of three drugs, diazepam, baclofen, and dantrolene sodium, for the control of spasticity is discussed. Diazepam by central action has a muscle relaxant effect. The antispastic effect of baclofen is exerted to a large extent at a spinal level and differs from that of the commonly used general depressants that preferentially inhibit polysynaptic reflexes. Dantrolene sodium acts directly on the muscle fibers distal to the end plates, probably by influence on the excitation/contractions. These differences in site of depressive effects dictate the clinical application of the drug depending on the nature of motor disorder. 8 references.

004842 Lacoursiere, Roy B. Veterans Administration Medical Center, Topeka, KA 66622 **Psychopharmacological precautions in the right to refuse medication.** American Journal of Psychiatry. 137(7):856-858, 1980.

Three psychopharmacological issues concerning patients' right to refuse medication are discussed (the therapeutic time lag that occurs between initiation of drug therapy and development of therapeutic effects; the deterioration time lag that occurs from time of drug discontinuance until symptom recurrence or exacerbation; and effects of abrupt medication withdrawal). It is contended that if one accepts the right to refuse psychotropic medication, one must also accept the responsibility for that decision, and the deleterious consequences can be subtle. It is claimed that in general, the decision to refuse medication will prolong the period of dangerousness to self and/or others, and the length of hospitalization, and that the decision to refuse further psychotropic medication by patients who show no immediate dangerousness to themselves and/or others means the deleterious effects of the decision may occur after the patient is discharged. The brief literature on withdrawal reactions from neuroleptics, tricyclic antidepressants, antiparkinsonian medications, and lithium is cited. 10 references.

004843 Ladwig, Karl-Heinz. Ottingenstrasse 36/II, D-8000, Munich 22, Germany **/Anamnesis of sleep in the internal medicine hospital./** Nachtschlafanamnese in der internistischen Klinik. Medizinische Klinik. 74(51/52):1957-1961, 1979.

An anamnestic sleep questionnaire was developed and administered to 41 unselected but seriously ill hospitalized patients, 23 to 71 years old. Data analysis suggests that disturbed sleep is a universal problem and is significant at the clinic. Frequently fragmented sleep appears to be the most important form of disturbed sleep. Answers to often used and stereotyped questions concerning sleep conditions are neither correlated to the subjective status nor to objective behavioral data on sleep. Physical/technical stimulus patterns appear to be of minor importance to internal conditions in sleep disturbance. Fear of medical investigation and expectation of an uncertain future were high. The need for psychosocial guidance for hospitalized patients is noted. The medication rate for hypnotics and tranquilizers is high, and the percentage of patients who are engaged in exercising consciously presomnic behavioral patterns is low. Patients who demonstrate a negative attitude toward soporifics perceive side-effects on a significantly larger scale than do positively motivated patients. A negative attitude toward these drugs has no behavioral consequences. 18 references. (Journal abstract modified)

004844 Lapierre, Y. D. School of Medicine, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada **Psychopharmacotherapy: a review of twenty years.** Psychiatric Journal of the University of Ottawa. 4(1):73-80, 1979.

Developments in psychopharmacotherapy over the last 20 years are reviewed. Research studies on drugs used in neurotic conditions (meprobamate, benzodiazepines, anxiolytics), antidepressant drugs (iminodigenzyls, dibenzocycloheptenes, hydrazines, amitriptyline, clomipramine), drugs for manic-depressive syndrome (lithium), neuroleptic drugs (propylamino derivatives, propylpipserazine derivatives, alkylpiperidyl derivatives, butyrophenones, and thioxanthenes) are summarized. Future advances in psychopharmacotherapy for depression, manic-depressive illness, and schizophrenia are suggested. 52 references.

004845 Linde, O. K. Pfalzklinik Landeck, Weinstrasse 100, D-6749 Landeck, Germany **/Investigation of unknown medication taken before hospital admission./** Untersuchungen zur anonymen praklinischen Medikation. Pharmakopsychiatrie Neuro-Psychopharmakologie. 12(3):286-290, 1979.

Patients with diagnoses of alcoholism (29), psychoses (30), depression (20), drug addiction (9), cerebral atherosclerosis (14), epilepsy (5), neurosis (2), and other diagnoses (5) were studied to determine the incidence of ingested preclinical medication. Results show that only one fourth of the statements given by patients or accompanying persons regarding preclinical medication were true. In about 66% of the cases one to five drugs were not stated during the first interview, while in 10% of the cases more drugs were stated than had actually been taken. Among the substances which remained anonymous, the main shares were represented by benzodiazepines (28%), narcotic drugs (19%), neuroleptics (15%), and alcohol (15%). The highest quota of false statements was found among the addicts (100%), followed by alcoholics (66%), patients suffering from

psychoses (52%), and depressive patients (47%). 7 references. (Journal abstract modified)

004846 Ling, Walter; Klett, James C.; Gillis, Roderic D. Virginia Medical Center, Sepulveda, CA 91343 **A cooperative clinical study of methadyl acetate: II. Friday-only regimen.** Archives of General Psychiatry. 37(8):908-911, 1980.

An open clinical trial was conducted of the feasibility of maintaining heroin addicts via methadone hydrochloride on Monday through Thursday, methadyl acetate on Friday, and no drug on Saturday or Sunday. A group of 65 heroin patients received this treatment schedule, while 71 were assigned to a daily methadone comparison group. The starting dose of methadyl acetate was identical to the previously established dose of methadone, but was flexible within limits thereafter. More patients in the experimental group failed to complete the full 40 weeks of treatment, mostly because they claimed the medication was not holding. Although this particular use of methadyl acetate on Friday to provide a drug free weekend does not appear to be widely applicable clinically, the fact that at least some patients tolerated the schedule with little or no illicit drug use or obvious discomfort suggests that the strategy is viable and should not be discarded. 2 references. (Author abstract modified)

004847 Marholin, David, II; Touchette, Paul E.; Stewart, R. Malcolm. Touchette: Educational-Psychology Research, Kennedy-Shriver Center, 200 Trapelo Road, Waltham MA 02154 **Withdrawal of chronic chlorpromazine medication: an experimental analysis.** Journal of Applied Behavior Analysis. 12(2):159-171, 1979.

Since approximately 50% of all institutionalized, mentally retarded adults receive psychotropic medication to control inappropriate behavior, an experimental analysis was made of the withdrawal of chronic chlorpromazine medication. Behaviors exhibited by five retarded adults were formally observed while they were on and off medication. Each S had been receiving chlorpromazine for 6 or more years prior to the start of the study. The drug was withdrawn and readministered using a double-blind B/A/B (drug/placebo/drug) design. Effects were highly individualized. Some desirable behavior emerged when chlorpromazine was discontinued. 37 references. (Author abstract modified)

004848 Mauk, Michael D.; Olson, Gayle A.; Kastin, Abba J.; Olson, Richard D. Dept. of Psychology, University of New Orleans, New Orleans, LA 70122 **Behavioral effects of LH-RH.** Neuroscience and Biobehavioral Reviews. 4(1):1-8, 1980.

The physiological and behavioral effects of luteinizing hormone releasing hormone (LH-RH) are reviewed. The structure and localization of the hormone are discussed. LH-RH facilitates mating behavior in rats, but clinical studies of LH-RH have been inconclusive. 150 references. (Author abstract modified)

004849 Molcan, J.; Guensberger, E. Medical Faculty/Komensky Univesity, Mickiewiczowa II, Bratislava, Czechoslovakia **/The connection between pharmacotherapy and psychotherapy in psychoses./** Verhaltniss der Pharmakotherapie und Psychotherapie bei Psychosen. Agressologie. 20(D):283-285, 1979.

An overview on current objections to the combined use of pharmacotherapy and psychotherapy in the treatment of psychoses is presented. The argument against the use of pharmacotherapy in treatment of psychoses stems from the perception that use of pharmaceutical agents may dampen and diffuse the original symptomology. However, an argument is made that this view is biased and that the combination of psychotherapy and pharmacotherapy may assist in the treatment of the patient by alleviating anxieties and various other symptoms that may hinder the psychotherapeutic process. (Journal abstract modified)

004850 no author. no address **/The use of bromocriptine for numerous disorders./** ...and in Europe for long list of dopamine disorders. Medical World News. 20(12):52-53, 1979.

The various uses of bromocriptine, an ergot derivative which acts by prolonged stimulation of dopamine receptors, are examined. Studies indicating that bromocriptine is effective in treating acromegaly, Parkinson's disease, postpartum lactation, hypogonadism, male infertility, and pituitary tumors are cited. Other studies indicate that it has limited value for premenstrual syndrome, hypertension, anorexia nervosa, mania, and female infertility.

004851 no author. no address **Final task force report on bioavailability and bioequivalence of psychotropic drugs.** Psychopharmacology Bulletin. 16(3):9-13, 1980.

The final report of the committee on bioavailability and bioequivalence of psychotropic drugs of the American College of Neuropsychopharmacology is presented. It is noted that psychoactive drugs require titration for the individual patient to achieve maximum therapeutic benefit and to avoid symptoms of withdrawal and/or side reactions. It is the opinion of the task force that the proclaimed difficulties in bioavailability assessment of psychotropic drugs is related to the minimal effort which has been expended in the bioavailability evaluations of these drugs. The task force concluded that it would be most undesirable to use multisource psychotropic drug products interchangeably without establishment of their bioequivalence. It is the task force's belief that without such federal requirements there may in fact be bioinequivalence among these psychotropic drugs occurring either now or in the near future, due to the repeal of antisubstitution laws in over two thirds of the states in the United States.

004852 Oules, Jean; Boscredon, J.; Concina, M. Centre Hospitalier, F-82000 Montauban, France **/The use of minaprine for hospitalized psychiatric patients and outpatients./** Utilisation de la minaprine en psychiatrie hospitaliere et ambulatoire. Psychologie Medicale. 11(1):225-231, 1979.

The effect of minaprine was tested in an open study of 33 cases and in a cooperative double-blind trial of 49 cases. The dihydrocholorate of 2-morpholino-3-ethylamino-4-methyl-6-phenyl pyradizine or 30038 C.B. is neither an antidepressant nor an anxiolytic and has no amphetamine type action. Due to its clear psychostimulative action, it can be given alone or in association, with other drugs, particularly antidepressants, in all states where passivity, indifference and asthenia predominate. It was found to improve sexual disorders such as the diminution of the libido and premature ejaculation. It was also observed to positively modify the physical feeling of depression due to psychostimulant action and its occasional euphoric effect. A psychostimulant in the broad sense of the word, it proved to have good tolerance and is considered to be useful both for the specialist and the general practitioner. 4 references. (Journal abstract)

004853 Parnas, Josef; Flachs, Helga; Gram, Lennart. Dept. of Psychiatry, Kommunehospitalet Oster Farimagsgade 3, DK-1399 Copenhagen K, Denmark **Psychotropic effect of antiepileptic drugs.** Acta Neurologica Scandinavica. 60(6):329-343, 1979.

Eighteeen controlled studies investigating the psychotropic effect of antiepileptic drugs are critically reviewed. The neurochemical evidence for existence of psychotropic properties is still speculative. It seems questionable on the basis of this survey

that there exist genuine psychotropic effects of antileptic drugs, which are not related to antiepileptic efficacy and/or differences in toxicity. 32 references. (Author abstract)

004854 Poldinger, Walter; Schmidlin, Paul E. no address / **Index of Psychopharmacology.**/ Index psychopharmacorum. 5th ed. Bern, Hans Huber, 1979. 104 p. DM26.

A revised and augmented edition of a trilingual (English, German, and French) index of psychopharmacological terms is presented. Substances are arranged according to pharmacological and clinical categories, as well as by a reference system according to chemical structures. Alphabetical listings consider generic terms as well as the commercial, proprietary, and familiar trade names; however, composite preparations of more than one active ingredient are not listed -- only the single substance drugs. Psychotonic drugs, the sympathomimetic amines, stimulants without psychiatric indications, and pure sedatives and hypnotics have also been omitted to keep the listing manageable. The conventionally accepted classifications (neuroleptic, antidepressant, and tranquilizer) have been retained, and breakdowns include the derivatives of the families of basic substances.

004855 Ravn, J.; Scharff, A.; Aaskoven, O. Indre Ringvej 23/III, DK-7000 Fredericia, Denmark /**20 years' experience with chlorprothixene.**/ 20 Jahre Erfahrungen mit Chlorprothixen. Pharmakopsychiatrie Neuro-Psychopharmakologie. 13(1):34-40, 1980.

Twenty years of experience with chlorprothixene, the first neuroleptic of the thioxanthene group which was marketed in 1959 under the trade names of Taractan and Truxal, are reported. Study of 801 publications, including 542 clinical works yielded 108 publications that were suited for analysis. Data were obtained on 11,487 patients, from which it is concluded that chlorprothixene has been proven a broad spectrum neuroleptic with good therapeutic effects. Side-effects, especially extrapyramidal symptoms, appear rarely. Among the 11,487 patients, only 1.02% showed such symptoms and of these only 0.05% had tardive dyskinesias. Evidence suggests that these are schizophrenic patients showing extrapyramidal symptoms without having received neuroleptics. 19 references. (Journal abstract modified)

004856 Richards, William A. 2516 Talbot Road, Baltimore, MD 21216 **Psychedelic drug-assisted psychotherapy with persons suffering from terminal cancer.** Journal of Altered States of Consciousness. 5(4):309-319, 1980.

An overview of an experimental program of psychedelic drug assisted psychotherapy for terminal cancer patients suffering from psychological stress and depression is reported. Over a 12 year period, 91 oncology patients have been treated: 50 with lysergic acid diethylamide (LSD), 40 with dipropyltryptamine (DPT), and one with psilocybin. Therapy was usually conducted on an individual basis and had an existential/humanistic orientation. Therapeutic procedures prior to drug administration, during the drug experience, and after drug effects had abated are described in detail. Three general types or levels of experience were reported by patients which were potentially significant in facilitating decreases in psychological distress and increases in self-actualization and personal growth: psychodynamic experiences such as regression to childhood or infancy with literal or symbolic reexperiencing of emotionally charged materials; symbolic archetypal phenomena often with mythical/religious themes of purification, acceptance, and forgiveness; and mystical consciousness often described as death and rebirth and merging of the self with an all encompassing unity. 16 references. (Author abstract modified)

004857 Rush, A. John. Dept. of Psychiatry, University of Texas Health Science Center, Dallas, TX **Drugs and psychotherapy in the treatment of depression.** Psychopharmacology Bulletin. 16(2):60-62, 1980.

Studies comparing the effects of drugs and psychotherapy in the treatment of depression are reviewed, and interactions between the effects of drugs and psychotherapy are discussed. None of the studies reviewed shows a positive interaction between psychotherapy and chemotherapy regarding either symptom or social adjustment measures alone, although an interaction is suggested if the measures are combined. Available data suggest that the targets of various psychotherapies differ, and indeed, their actual effects are related to the objective chosen. There is no convincing evidence yet for a prophylactic effect of psychotherapy or for a positive synergistic effect of combined psychotherapy and chemotherapy.

004858 Schmidt, Chester W., Jr. Dept. of Psychiatry, Baltimore City Hospitals, 4940 Eastern Avenue, Baltimore, MD 21224 **Biomedical methods in the treatment of sexual disorders.** Psychiatric Clinics of North America. 3(1):189-199, 1980.

Past and current experience in the use of biochemical agents to treat sexual disorders is reviewed, and speculations on the future developments, in chemotherapy are made. Although human sexual experience can be modified by a variety of chemical means, there are to date only a few conditions which will reliably respond to chemical treatment with androgens, estrogens, antipsychotic agents, antianxiety drugs, antidepressants, sedative hypnotics, antiandrogens, and street drugs. Current research suggests, however, that sex hormone aberrations may contribute to a number of sexual disorders thought to be of psychogenic etiology, and additional studies are needed on the effect of testosterone on the male and female libido. Future biochemical treatment will follow developments in brain neurochemistry and bring about combinations of psychopharmacologic and psychotherapeutic methods. 26 references. (Journal abstract modified)

004859 Schooler, Nina R. NIMH, 5600 Fishers Lane, Rockville, MD 20857 **Priorities for treatment assessment research (TAR) in clinical psychopharmacology.** Psychopharmacology Bulletin. 16(2):54-55, 1980.

Priorities for treatment assessment research, a major research issue of the U.S. Alcohol, Drug Abuse, and Mental Health Administration, defined as research which generates evidence on both the efficacy and safety of treatments directed at persons with defined disorders, are described. Results of questionnaires completed by 28 professionals in the field of clinical psychopharmacology are discussed in terms of the following areas: 1) the extension of established treatments to new diagnostic groups; 2) extension of assessment studies to determine long-term safety and efficacy; 3) adverse effects; 4) development of increased specificity of indication for drug treatment; 5) studies of combinations of treatment modalities; 6) methodological prerequisites to research; and 7) research organization and funding.

004860 Slovenko, Ralph. Wayne State University, Detroit, MI 48202 **On the legal aspects of tardive dyskinesia.** Journal of Psychiatry Law. 7(3):295-331, 1979.

The tradeoff between psychosis and tardive dyskinesia and the legal implications of prescribing medication that causes this disturbance are examined. It is contended that of the various drug therapies, antipsychotic medication is presenting novel twists to old issues in law and psychiatry. From what is known, the benefits of such therapy are high, but so are its risks. The legal issues involved in the decision-making process include standard of care, informed consent, the right of institutionalized patients to refuse treatment, the statute of limitations, and causal nexis. 13 references. (Author abstract modified)

004861 Squyres, Elton M.; Chabaud, Suzanne; Jacobs, Keith W. Loyola University, New Orleans **PCPA and serotonin: a bibliography of biogenic amine research.** JSAS/Catalog of Selected Documents in Psychology (APA). 9(May):28, 1979. MS. 1840, 70 p. paper:$8; fiche:$2.

A collection of 860 journal and book citations concerned with the manipulation of serotonin, primarily by administration of p-chlorophenylalanine (PCPA) is presented in a bibliography. Articles citing other drugs in the inhibition of serotonin and related neurotransmitters have also been included, as have studies relating to the depletion of serotonin and methods for determination of serotonin levels. Compilation of this bibliography has been largely the result of computer based searches of Index Medicus from 1950 thru 1977 and Psychological Abstracts from 1960 thre 1977. A comparison against reference lists from key sources suggests that this bibliography is more than moderately comprehensive. (Author abstract modified)

004862 Stimmel, Barry. no address **Cardiovascular effects of mood-altering drugs.** New York, Raven, 1979. 279 p. $29.90.

The cardiovascular effects of mood altering drugs (including alcohol, marihuana, hallucinogens, morphine, heroin, amphetamine, cocaine, caffeine, nicotine, barbiturates, benzodiazepines, phenothiazines, and antidepressants) on the central nervous system are described. Cardiac complications, particularly of the phenothiazines and the tricyclic antidepressants, especially with regard to effects on cardiac rhythm and conduction, are discussed.

004863 Vogt, Marthe. Agricultural Research Council, Institute of Animal Physiology, Babraham, Cambridge CB2 4AT, England **The impact on neurology of 40 years' advances in pharmacology.** Brain. 102(3):445-459, 1979.

Progress in clinical pharmacology in the last 40 years is discussed, with emphasis on the treatment of mental illnesses. The role of catecholamines, histamine, acetylcholine, amino acids, and other putative neurotransmitters in the etiology and treatment of schizophrenia and depression is considered. Research on peptides, (including substance-P, enkephalins, endorphins, ACTH, somatostatin, thyrotropin releasing hormone, gastrin, vasoactive intestinal peptide, neurotensin, bonmbesin, and angiotensin) is briefly summarized. 44 references.

004864 von Littrow, C. Direktionsbereich Forschung des VEB Arzneimittelwerk, Dresden, Germany **Tisocromide -- a psychopharmaceutical with antidepressant.** Tisocromid -- ein Psychopharmakon mit Antidepressiver Wirkung. Agressologie. 20(D):299-302, 1979.

The pharmacological and clinical properties of tricyclic antidepressant agents such as tisocromide, imipramine, desipramine, clomipramine, trazodone, viloxazine, mianserin, and nomifensine are discussed. During experiments with animals in the laboratory, tisocromide distinguished itself due to its cholinergic effect as well as its sedative, muscle relaxant, and analgestic properties. The first clinical experiments conducted by Federbusch and Feller on patients with depressive syndromes showed behavior altering properties which occurred in two phases: the first phase lasting 2 weeks stimulated the psychomotor symptomatology and the second phase normalized affective and emotional reactions. Additional studies by Nahunek on 100 patients with endogenous depression indicated 60% success in treatment with tisocromide. Results of these studies indicate that tisocromide is an effective agent in the treatment of depressive syndromes.

004865 Welbel, Leszek. Instytut Psychoneurologiczny, A1. Sobieskiego 1/9, 02-957 Warsaw, Poland **/Difficulties in evaluating the effects of pharmacological treatment in schizophrenia./** Trudnosci oceny wynikow farmakologicznego leczenia schizofrenii. Psychiatria Polska. 14(1):51-57, 1980.

The use and difficulty of assessing the effectiveness of pharmacological compounds in the treatment of schizophrenia is discussed with emphasis on uncertainties in the diagnosis of schizophrenia, methodological difficulties, methodological limits, and recommendations for the future. The difficulties in diagnosis have to do with clinical recognition of the syndrome, the determination of the state of illness at the time of treatment, demographic factors influencing treatment, nonbiological factors, and the use of psychotherapy and sociotherapy. Methodological problems take into account such aspects as difficulties in classification, the determination of which pharmacological compound is to be tested, at what dose, the use of placebo, the taking into account of previous therapy, interaction of drugs, evaluations of results, biological methods, and data processing of results. Methodological limits focus on legal restrictions, ethical restriction, criteria for selecting patients to be tested and the number that will provide a representative sample, blind studies, personnel needed during time of testing, and cost of testing procedures. Recommendations include the need to work out a more systematic method of evaluation, stricter legal controls, and a more widespread familiarity with test results among psychiatrists and clinicians. 37 references. (Journal abstract modified)

004866 Wells, Frank O. 38 Westerfield Road, Ipswich, Suffolk IP4 2UT, England **/The abuses of barbiturates./** Is your sleeping tablet really necessary? Journal of the Irish Medical Association Supplement. 72(12):15-18, 1979.

At the International Symposium titled held in Dublin, February 1979, a paper was presented which discussed a program established by the Ipswich Local Medical Committee which encouraged physicians to reduce the use of barbiturates for their patients. The dangers in the overuse of barbiturates include both a psychological and physical dependence. It is suggested that a gradual change from barbiturates to diazepam or another benzodiazephine will relieve the patient's dependency and insomnia. Insomnia should be regarded as a social inconvenience, or at worst a symptom of underlying pathology. Therefore prescribing the use of barbiturates should be limited to short periods of time. Also patients should realize that there are other ways of confronting stress and anxiety than pills.

004867 Wiatt, Alexander L.; Ornato, Joseph P. Outpatient Dispensing, McDonald Army Hospital, Fort Eustis, VA 23604 **Outpatient utilization of diazepam in a military hospital.** Military Medicine. 145(6):394-396, 1980.

The use of diazepam in an outpatient military hospital setting was investigated to further study the controversy over the frequency of use of these minor tranquilizers. Outpatient records of 58 patients presenting to the hospital with diazepam prescriptions or refill requests were examined. Mean duration of therapy was 38 months, while the average amount estimated to have been consumed was 12 mg per day, some 3 mg a day less than that which had been prescribed. Although a few specific instances of misuse were noted, most patients appeared to be using the medication in moderation over relatively long periods of time. 15 references.

004868 Yermolina, L. A. Otdel oligofrenii Moskovskogo NII psikhiatrii MZ RSFSR, Moscow, USSR **/The use of metabolic preparations in studies of mild forms of mental deficiency./** O primenenii preparatov metabolicheskogo deystviya dlya isucheniya legkikh form intellektual'noy nedostatochnosti. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova. 80(3):439-443, 1980.

The efficacy of metabolic preparations in the treatment of children with mild forms of oligophrenia and mental retardation

of an organic nature was studied. The substances piriditol, pantogam and piracetam were used in treating 200 children aged from 7 to 11 years. Results show the potential of these substances in relation to cognitive activity in cases of mental deficiency. 5 references. (Journal abstract modified)

004869 Yesavage, Jerome A.; Fill, Norman M.; Rosenbaum, C. Peter. Psychiatric Intensive Care Unit, Palo Alto Veterans Administration Hospital, Palo Alto, CA **Psychopharmacology in the setting of a psychiatric intensive care unit.** Psychopharmacology Bulletin. 16(2):14-15, 1980.

Principles of psychopharmacotherapy in the setting of a Veterans Administration psychiatric intensive care unit are discussed, and results of a survey of drug use in this unit are presented. Results of a survey of 30 consecutive admissions to the unit show that 28 of 30 Ss received neuroleptics. Twenty of these 28 received fluphenazine in doses which ranged from 5 to 120mg/day. In 21 months of using fluphenazine as first choice neuroleptic in over 600 patients, there have been no deaths or medical emergencies due to medications. Results indicate that patients who had been admitted involuntarily for being dangerous to others as opposed to those who were admitted as gravely disabled under California law received more neuroleptic. 5 references.

AUTHOR INDEX

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